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TREATMENT OF INJURIES TO THE KNEE JOINT*

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INJURIES to the knee joint may be discussed under the following three headings: diagnosis, treatment of surrounding structures and treatment of the joint itself. The third consideration, which is the most important, is the aspect of treatment that is usually neglected.

The basis of all treatment of the knee joint is an appreciation of the physiology of the knee and of how it is disturbed by injury to the joint. There is a mistaken idea that various ligaments stabilize the knee joint. The only two positions in which the ligaments stabilize the joints in living human beings are complete extension — as when one is standing at military attention — and complete flexion, as when one is in a full squat. These are unusual positions.

It is perfectly true that in the cadaver, the ligaments stabilize the knee joint. This discussion, however, applies to the physiology of the knee joint in human beings, not to that in cadavers — in other words, to dynamic anatomy, not static anatomy.

In uninjured persons stabilization of the knee joint in any degree of flexion is accomplished by co-ordinated muscle action of the surrounding muscles. If, for any reason, that action is disturbed, so that one group of muscles acquires power superior to that of another, the knee joint becomes unstable, whether or not there is any lesion of the joint ligaments. The ligaments serve to prevent gross displacements.

I can state factually what happens when the knee joint is injured, but I cannot adequately explain it. Any injury to the intra-articular portion of the knee joint is associated with a rapid hypotonia that is relatively selective for the extensor mechanism of the joint and involves the rectus and the vasti muscles. The flexor group of muscles is also involved, but to a mild degree. The extensor group is implicated to such an extent that a palpable difference in tone can be demonstrated within two hours after injury and visible evidence of atrophy is present within five days after injury. This point is too frequently not given adequate weight, mainly because the patient usually rolls up his trousers to disclose the knee joint. No patient should have anything covering his thighs during such an examination; he should be free of obscuring drapery from the hips down so that the thighs can be examined for any visible difference in size or contour, such as flattening of the rectus muscle, and palpated to determine the difference in tone, both in the relaxed state and in that of attempted contraction. The thighs should then be measured, at a definite level above a given anatomic landmark, so that the level will be exactly the same on the two sides. If there is no visible or palpable hypotonia or atrophy and no measurable atrophy, there is probably no lesion involving the knee joint, and it can be assumed that the lesion lies outside the joint. If there is palpable and visible hypotonia and measurable atrophy in the thigh muscles soon after injury, the difficulty lies within the joint. If that fact is remembered, one will already have gone a long way toward clearing up the diagnosis of obscure lesions in the knee joint.

The second point to remember is that any patient who develops fluid in the joint within hours of the injury does not have a traumatic synovitis but has a hemarthrosis. Whatever the diagnosis, it must explain the hemarthrosis. The habit of calling a collection of fluid within the knee joint a traumatic synovitis because no definite abnormality is observed is a serious mistake, because it implies that the joint has merely been irritated and that synovial fluid has collected. Synovial fluid collects in the knee joint over a period of days or weeks as a result of trauma, not over a period of hours. The condition must therefore be explained on the basis of bleeding into the joint.

The third point in diagnosis of these lesions is adequate examination, the first part of which consists in inspection, as pointed out above. Range of extension is a primary consideration. If the patient

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is seated, with the heel of the extended leg on the examiner's knee, and told to relax, the knee joint either goes into complete extension or remains in partial flexion. Persistent flexion is due either to muscle spasm or to mechanical blocking in the joint. Flexion caused by muscle spasm may be secondary to fluid in the joint, which can be pushed into full extension without severe pain under slow pressure; on release of the pressure, the knee rebounds into flexion. The normal knee in full extension never rebounds when the pressure is released. If the joint cannot be brought into full extension by steady, slow, continued pressure because of either mechanical obstruction to extension or the severity of the pain occasioned, more than muscle spasm or fluid is involved — there is probably a mechanical derangement of the knee joint.

I find it utterly impossible to make an exact differential diagnosis when confronted with the various mechanical derangements of the knee joint that can occur. A diagnosis of mechanical derangement of the knee joint is made on the basis of the following: a history of injury; hypotonia in the thigh muscles, with or without atrophy, depending on whether hours or days are involved; the rapid accumulation of fluid after injury; and inability to hyperextend the knee joint slowly and gradually into extension, as pointed out above. The injury may be a torn meniscus, a pinched fat pad, which is incidentally a real lesion, or a strain of the ligaments — that is, a mechanical derangement outside the knee joint. Sprains of the ligaments, unless accompanied by hemarthrosis, are not accompanied by hypotonia and loss of thigh contour. When actual ligamentous tears occur they are evidenced by abnormal mobility of the joint in full extension — that is, the leg can be abducted on the thigh if the internal collateral ligament is torn and adducted if the external collateral ligament is torn. In the normal knee, neither abduction nor adduction of the leg on the thigh in full extension is possible, nor is rotation of the tibia on the femur in full extension or forward or backward movement of the tibia on the femur in flexion. The integrity of the various ligamentous structures can thus be tested.

Another frequent lesion is that involving the crucial ligaments, which is a less serious injury than those described above. In the last twenty years this injury was observed at operation in an appreciable percentage of cases, and surgical repair was undertaken in extremely few. I have never seen a patient with a tear of the anterior crucial ligament who, on the basis of a three-year follow-up study, showed any physiologic disturbance of joint function if the quadriceps mechanism had been restored by active treatment, although Dr. John Royal Moore, of Philadelphia, has told me of a case in a boxer, who depended on his footwork for success, in which surgical intervention was necessary.

The posterior crucial, which is the more important ligament, keeps the femur from going unduly forward during weight bearing; the anterior merely keeps it from going backward in hyperextension — an unusual situation. During walking, the tendency is for the femur to slide forward on the tibia when the knees are flexed and weight is borne. The posterior crucial ligament therefore has more functional value than the anterior crucial. The posterior crucial ligament is completely torn when complete dislocation of the knee joint occurs. It is a startling fact that in such dislocation marked instability after reduction and restoration of the muscular mechanism of the thigh is not a characteristic finding.

I therefore recommend much less attention to injuries of the crucial ligaments than is usually accorded them. They represent an internal derangement of the knee joint, without mechanical block. But, more to the point, they represent loss of tone and atrophy in the quadriceps group of muscles, which should be the center of attention for treatment.

Simply because the diagnosis of injury to the knee joint has been made is no reason for an operative procedure. The real physiologic disturbance is hypotonia and atrophy of the quadriceps group of muscles. Attention should be centered on that disturbance.

The number of operations devised to repair ruptures of the crucial ligament is legion. Each one has been devised because the preceding ones have proved to be unsatisfactory. And the end is not yet in sight. The point of attack is wrong, emphasizing a torn structure rather than the physiologic disturbance created by the injury. The less operating done on crucial ligaments and the more attention devoted to restoring tone and power to the quadriceps group, the better off the patient will be. In other words, these injuries, in my opinion, call for constructive conservative therapy — I regard the terms "intelligent" and "constructive," as synonymous.

The diagnostic feature of meniscus injury is a sudden, twisting effort, with the knee flexed, that results in localized pain on the inner or outer side of the knee joint, followed sometimes (but not always) by a rapid accumulation of fluid. Tenderness at the site of the pain, with or without locking of the knee joint, is observed. When the cartilage separates, it may tear loose from its ligamentous attachments to the edge of the tibia, in which event the rupture is through vascular connective tissue. The cartilage may be displaced within the joint. If it remains within the joint, there is a mechanical locking, and the knee will not fully extend because a block of fibrocartilage lies between the tibia and the femur; full extension cannot be obtained, even with an anesthetic. Such a joint must be unlocked. It is pointless to immobilize such a joint in the

locked position. Before it is immobilized, if that form of therapy is to be used, the joint must be unlocked by operation or by manipulation. I do not believe that operation should be performed on a patient with a primary injury until manipulative reduction has been tried. Any manipulation should be done under an anesthetic, for several reasons. In the first place, the patient's muscles must be completely relaxed — otherwise, there is muscle resistance to the manipulation, and failure is probable. Secondly, under anesthesia the manipulation can be more carefully done, repeatedly if necessary, with a minimum of trauma to the joint. Thirdly, the manipulation under anesthesia will not cause pain and distress to the patient, increasing his protective reflex safeguarding the joint and interfering with later functional activity.

The method of reduction is simple. The hip and knee are flexed at right angles. The tibia is rotated loosely inward and outward on the femur in the flexed position, under anesthesia. I prefer intravenous anesthesia because it gives excellent relaxation. Having employed rotation, one loosely abducts and adducts the tibia on the femur in the flexed position. Following this, the knee is brought into sudden extension. The purpose is the same as in shelling peas: the pea is popped out of the pod by pressure between the fingers. The meniscus is the pea, the joint is the pod, and the femur and the tibia are the two fingers. Once the cartilage has been "popped" from its locked position to the periphery of the joint, it cannot go back into the joint as long as the knee is extended.

If the patient's knee is not locked, although he has the signs of a meniscus tear, I believe in radical surgery, in the sense that any procedure undertaken should be complete and thorough. I also believe that any surgeon who performs an unnecessary operation is foolish. No patient with a meniscus lesion whose knee joint is or can be unlocked should be operated on for a first injury. I admit that, on the basis of paper logic, operation is the wisest and most sensible procedure. Once the meniscus is removed, there should never be any more trouble. Perhaps some surgeons never have complications after a knee-joint operation. I sometimes do. Some patients never get pneumonia, or atelectasis or thrombophlebitis and embolism. But some do. Some patients are successful in restoring quadriceps function and stability after operation. But some are not. If the knee joint in a case of primary injury cannot be unlocked the patient should be operated on — not within a week or a month, but as soon as possible.

When the joint can be unlocked or has never been locked and the meniscus is probably involved because of the symptomatology, the knee joint must be kept extended. No activity should be permitted in a patient with a knee joint that is moving, because constant movement will cause continuous damage. On the other hand, the quadriceps group of muscles is developed solely by exercise. The surgeon seems to be between the devil and the deep sea — the patient cannot exercise his knee, but he must develop his quadriceps.

The problem is not too difficult. The patient must be kept from moving his knee, but he must be made to walk. A plaster or other encasement from ankle to groin in extension does the former, and every hour or oftener, he walks progressively increasing distances without crutch or cane. The substitute for such co-ordinated muscular activity is the quadriceps-contraction exercise — a substitute, but a poor one, because it exercises only the quadriceps group of muscles. What is desired is co-ordinated action by all the muscles of the thigh. When the patient contracts the quadriceps, he selectively exercises a single group of muscles. This is not physiologic quadriceps function. Walking with the knee immobilized must be practiced long enough for the torn ligamentous attachments to reattach, roughly for four weeks; then the plaster is removed, and normal function is started. If the procedure is properly carried out, the patient does not add the atrophy occasioned by disuse to the primary reflex atrophy and hypotonia. He exercises the quadriceps group of muscles as part of a co-ordinated muscle action, and as a result he does not have a weak and atrophied thigh and does not complain that if he turns suddenly his knee "goes out" from under him.

The "giving way" of the knee is usually due not to a residual lesion in the joint but to the facts that muscle support of the joint is inadequate in the quadriceps group and that the joint is thereby rendered unstable. When the plaster encasement is removed the patient is not taught to bend his knee but to develop extensor power, which is where his defect lies. His flexor power is unimpaired.

What is it that makes immobilized joints stiff? There is a good deal of vague and misleading talk about contractions and adhesions. Actually, the patient is suffering from loss of elasticity in and thickening of the capsular structures. This results from loss of efficiency of the minute circulation, secondary to absence of normal muscular activity — the essential factor in maintaining the circulation at an efficient level. A joint does not have to move to remain supple and limber. The muscles that ordinarily move the joint must be kept moving for the minute circulation of the part to approach normal. Ligaments will not be thickened and lose elasticity, leading to stiffness, nor will the mesotenon and paratenon become thick and inelastic secondary to circulatory stagnation.

A tendon does not lie loose and unconnected with the surrounding tissues. It moves because the soft parts — represented by mesotenon or paratenon — are thin, extremely elastic and almost weblike. If they are subjected to chronic vascular stasis, a

cirrhosis is, in effect, produced, with a thickening of the structure and loss of elasticity.

The problem is not one of adhesions or contractures but one of circulation, particularly of the minute circulation. That is why normal and co-ordinated muscular activity is so important, apart from its function in the stabilization of the joint.

When the plaster encasement is removed in a case of knee-joint injury, the patient must extend his knee. When he is being taught to walk, instead of being told to be sure to flex the knee at each step, he is instructed to push the knee backward at each step. This is a means of making the quadriceps muscle work. The flexion function returns routinely on normal use.

Straight-leg raising is another excellent method of cultivating extensor function. But the best one is walking, which is a normal and co-ordinated muscle exercise. The patient is not concerned with the action of individual muscles; he practices co-ordinated action of the whole muscle group. (It may sound as though I am making a great deal out of a minor point; this is actually a major point, involving the whole basis of a normal physiologic functional exercise.)

If a patient with a knee joint must be operated on because of the nature of the original injury or because conservative therapy, as described, has failed, what should be done? I have been impressed over the years with the folly and impracticability of making a clear-cut and definite diagnosis in cases of internal derangement of the knee joint. I know that there are those who believe that the definite diagnosis of a single and specific lesion can be made; I am not among them.

When a knee joint is operated on for internal derangement, which is as far as I am willing to go in making a diagnosis, I explore the joint thoroughly. I do not make a peephole incision for removal of the meniscus, if that seems the probable difficulty. It can be done simply, of course. Instead, the joint is exposed from top to bottom. I operate without a tourniquet, since I do not believe that temporary anoxemia is of any help to the tissues. A high Trendelenburg position, to further adequate venous return, without a tourniquet, is accompanied by little bleeding.

After a parapatellar incision from the tibial margin to the upper limit of the suprapatellar pouch the patella is displaced to the outer or inner side of the joint. The knee joint is then flexed over the table, enabling visualization of the whole joint and permitting attempts to correct all pathologic conditions observed.

In a series of over 400 cases in which knee joints were so explored, injury to the internal meniscus alone occurred in only 30 per cent. In another 30 per cent at least one other lesion, such as a torn crucial ligament, a lesion of the synovial membrane or a fat-pad lesion, was discovered. In 40 per cent, from three to nine lesions in addition to that of the meniscus were observed.

Operation in these cases is therefore performed through a long, generous incision, which heals from side to side, not from end to end. The long incision has the same healing time as the short one, and does not entail any difference in postoperative regime from that used with a short incision.

It has been held by some that the knee joint must be kept perfectly quiet postoperatively because movement of the soft parts will interfere with healing. It is interesting that most studies of wound healing are made on the abdominal wall, which is under constant movement twenty-four hours a day with every respiratory movement; it cannot be kept quiet. But there is normally no difficulty in healing of the abdominal wall. It is true that if the patients cough, vomit or sneeze, the wound may not heal properly. The situation is identical in the knee joint. The knee joint can be kept moving but, metaphorically speaking, cannot be allowed to cough, sneeze or vomit. Overpushing of the joint movement, the use of violent or forced exercise, exercise to fatigue limits or beyond pain limits are contraindicated. But healing is aided by movement within physiologic limits. The joint should never be immobilized postoperatively — one of the reasons why knee-joint injuries and operations are associated, in the lay mind, with stiff knees is the fact that for many years it was routine to immobilize knees postoperatively for considerable periods. I am sorry to say that in some places this is still done. If a knee joint is immobilized postoperatively, there must be a valid excuse for the procedure, and the excuse cannot be the problem of wound healing. There is a physiologic limit to the amount of exercise permissible. In general, however, the more exercise obtained for the muscles activating the knee joint within those limits, the better off the patient.

When an injury to the meniscus has cleared up under conservative treatment and the joint is again injured two or three or more months later, the same conservative treatment is not repeated. If the meniscus tear involves the ligamentous structures uniting the meniscus to the margin of the tibia, it will practically always heal under the conservative treatment I have described. If the tear, however, is through the cartilage itself, as in a so-called "bucket-handle fracture," in which the tear runs the length of the cartilage, or if a tab is torn loose from the edge of the cartilage, the chances are that the lesion will never heal. That is a broad statement, but on the basis of all the evidence reported to date, a tear limited to the meniscus will not heal, although it usually heals if it is through the ligamentous structure. If, therefore, under conservative therapy for a supposed torn meniscus the patient becomes free from symptoms, and later has a recurrence of symptoms, it is to be assumed that the tear is through the cartilage and has not healed under

conservative treatment. The patient is then a fit subject for operation.

To make assurance doubly sure, is it wise to wait for multiple recurrences before resorting to operation? Such a course is the equivalent of locking the stable door long after the horse has escaped. By the time a patient has sustained such multiple incidents, he has badly damaged the articular cartilage of the joint. Such misguided conservatism simply contributes to progressive damage of the knee joint.

Although I am opposed to operating on a patient with a primary injury of the meniscus if the joint can be unlocked, there is no question in my mind that a second incident, and not the eighth or ninth, is the indication for operation. Conservative therapy is wasted on recurrences of the original injury.

Discussion

Dr. Ezra A. Jones (Manchester): I should like to ask concerning the value of treatment with x-rays. Do you think that air injection is of any value? Also, what is the percentage of injuries to the lateral meniscus as compared with those to the medial meniscus, if there is the same damage?

Dr. Murray: On the question of air injection, for the last twenty years, I have tried air injection, oxygen injection and air or oxygen combined with other roentgenographically demonstrable substances. The net result has been to make the problem of injuries to the knee joint doubly confusing, because of the extra shadows that the injection of air and opaque material demonstrates. Recently, in Sweden, a technic was developed by which air is injected and x-ray examination is made by coning down to a small concentrated area, such as the internal meniscus and the intercondylar notch, and the claim is made — I have seen some of the pictures, and I am investigating some of them now — that by that technic more specific abnormalities can be demonstrated. I am attempting to duplicate that story; otherwise, my experience is that all that air injections have done is to confuse the picture.

Regarding the question about the relative percentage of injuries to the internal and the external meniscus, roughly 15 per cent of cases occur in the lateral meniscus. Whenever the diagnosis of a lesion of the internal meniscus is made the joint is thoroughly investigated; 10 per cent of cases are bilateral. About 5 per cent of all meniscus lesions occur in the external meniscus alone.

Dr. Albert P. LaFrance (Laconia): I should like to ask Dr. Murray if, when he encounters an injury of the fat pad, he removes the fat pad extensively or treats the case conservatively, with the idea that the lesion may subside.

Dr. Murray: Fat-pad injuries have the same history that one ordinarily gets with a meniscus lesion. There is tenderness alongside the patella tendon and far forward on the joint line, right at the edge of the patella tendon. All the cases are treated conservatively for the first incident — that is, by resting the joint but at the same time exercising the muscles as described above and by enforced walking in plaster, followed by the development of the quadriceps muscle later. With a second occurrence — in other words, a second pinching incident — the joint is explored, the fat pad is removed and the patient is treated postoperatively as for any knee-joint injury.

A Physician: I am in accord with the stressing of the restoration of the quadriceps muscle for strength and function. I must admit that I believe in contraction to some extent, in addition to all the other things, such as early motion and normal use. I believe in exercising the quadriceps muscle, especially in teaching the patient to control the muscle while he is still in bed. Actually, I prefer to have the patient do quadriceps exercises preoperatively, to learn to use the muscle, and then learn to walk.

Dr. Murray: The exact criteria employed in this routine should be stressed. As pointed out above, the knee joint should not be permitted to "cough" or "vomit" or "sneeze." By this, I meant that premature weight bearing is comparable to coughing or sneezing after abdominal operations.

I like to let patients walk on the third day; I have had some who walked on the second day, and many walk only on the sixth or seventh day. None of them are immobilized. I try to get them to do straight-leg raising, muscle exercises and actual walking.

Dr. Robert R. Rix (Manchester): A diagnosis of internal derangement of the knee joint should not be lightly made, as Dr. Murray pointed out, because it is disconcerting to operate on a knee joint and not find anything. Of course, when a knee joint with a bucket-handle tear is opened, the injury is visible. But if the tear is in the posterior portion of the cartilage, out of sight, it cannot be seen. And it is therefore extremely important to make the diagnosis of the tear in the posterior end of the meniscus, so that the knee joint can be entered with confidence and the cartilage removed.

I want to ask Dr. Murray on what criteria he bases the diagnosis of posterior tear of the meniscus.

Dr. Murray (closing): The diagnosis is revealed by pain back of the knee joint on attempts to straighten the knee and by a point of tenderness behind the internal collateral ligament. This situation is one of the reasons why an incision allowing complete exploration of the joint is made. The incision starts at the top of the quadriceps pouch and is brought down around the border of and 2.5 cm. away from the patella, and then down practically to the tibial tubercle. The patella is displaced outside or inward. The anterior two thirds of the cartilage can be examined through the incision when the knee joint is fully flexed. The fat pad is then removed — it is completely removed in every knee-joint exploration. Operation is performed specifically for a fat-pad lesion, of course, but the pad is removed as a routine in operation for any other lesion because, if it is out, it can never subsequently be pinched, and because its removal permits a wide view of the joint, which is otherwise seriously handicapped by the fat pad, particularly if it is large.

With a history and a suspicion of a tear that cannot be seen, particularly in cases in which repeated incidents have occurred, the posterior part of the joint is explored. Formerly, such exploration had to be done through a separate incision, alongside the hamstrings. But recently, instead of the parapatellar incision, the incision is begun at the top of the quadriceps pouch and is a semicircular one that comes around the lateral or mesial aspect of the knee joint and forward to the tibial tubercle below the patella. This has two advantages. The skin incision lies over the lateral aspect of the joint, and exercise does not increase the tension on the sutures. The anterior skin flap is dissected forward, and the anterior capsule incision can be made close to the patella. If no lesion of the cartilage is observed, the capsular incision is closed and the joint is opened behind the collateral ligament, the posterior portion of the cartilage being inspected. Thus, only one skin incision — and therefore one source of infection — is involved.

RESULTS OF BILATERAL SUPRADIAPHRAGMATIC SPLANCHNICECTOMY FOR ARTERIAL HYPERTENSION*

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ARTERIAL hypertension, usually designated as essential hypertension, is a highly complex disease syndrome. Its manifestations are many and varied, making a true evaluation of any form of therapy extremely difficult. This is further complicated by the normal progress of the disease, which encompasses the extremes from a fatal termination in a few months to a seemingly benign course of many years. Arterial hypertension is never actually benign, however, and the term should not be used. Sooner or later, damage to the brain, heart or kidneys will surely result. The term "essential" is also a misnomer. The elevation of the blood pressure is not necessary, as was at one time believed, to ensure an adequate blood supply to the various organs of the body in the presence of arteriosclerosis.

Although the disease may principally affect the brain in one patient, the heart in another and the kidneys in a third, in all the common factor is a more or less continuous elevation of the blood pressure, both systolic and diastolic. An increase in the blood pressure — temporary, recurrent or continuous — can, of course, occur with a wide variety of pathologic conditions, such as cerebral trauma, basophilic adenoma of the pituitary body, adrenal tumors, coarctation of the aorta and chronic nephritis. In 1939 Page[1] listed forty-seven conditions causing or associated with an elevated blood pressure. The diagnosis of arterial or essential hypertension is really made by exclusion of all the other conditions that may present a somewhat similar picture. This paper considers only the surgical treatment of what is usually designated as "essential hypertension" and, in its severer form, "malignant hypertension."

RATIONALE FOR SURGICAL TREATMENT

The rationale for the surgical treatment of hypertension is dependent on one's conception of the disease, especially of its etiology. No one has yet been able definitely to establish the actual cause of arterial hypertension. I have accepted the renal humoral theory, best demonstrated by the brilliant experiments of Goldblatt,[2] who has conclusively shown that renal ischemia, or at least interference with its hemodynamic state, produces a continuous elevation of blood pressure without evidence of impaired renal excretion. Numerous workers have shown that such interference with the blood supply of the kidneys results in an excessive amount of a renal pseudoglobulin called "renin," which reacts with another pseudoglobulin, probably from the liver, named "preangiotonin" (the "renin-activator" of Page[1]) to form an active vasopressor substance called "angiotonin." This causes arteriolar constriction of sufficient degree to raise peripheral resistance throughout the body, with consequent elevation of blood pressure.

Numerous causes for a primary renal ischemia may exist, but I believe that in the majority of cases it is of neurogenic origin. It has been demonstrated experimentally that electric stimulation of the splanchnic nerves elevates blood pressure, presumably by constriction of the arterioles in the kidney, with resulting renal ischemia. It is my opinion that in human hypertension excessive stimulation through the splanchnic nerves causes similar changes in the renal hemodynamics. This abnormal stimulation of the splanchnic nerves originates, of course, in the autonomic centers of the brain. The activating stimulus may be psychic, reflex from stimuli originating in various parts of the body or chemical. It is known that normally such stimuli are constantly influencing the sympathetic nervous system. How, then, can one explain the abnormal excessive response, sufficient to cause a renal ischemia? I believe that it is a congenital abnormality in the autonomic nervous system whereby excessive responses are evoked by normal stimuli. In the majority of hypertensive patients this congenital tendency of the autonomic system to over-react — that is, to respond to a given stimulus by either greater or more prolonged vasoconstriction — is apparently inherited.

I believe that Raynaud's disease presents a comparable condition. Here, excessive responses to normal stimuli of the autonomic nervous system result first in repeated abnormal vasoconstriction of the peripheral vessels in the hands and feet. Later, with more continuous constriction, permanent vascular changes leading to gangrene occur. No one doubts the role of the autonomic nervous system in Raynaud's disease, since there is definite visual evidence of vasoconstriction following psychic stimuli or exposure to cold. My hypothesis is that in hypertension similar stimuli acting on the abnormally sensitive autonomic centers for the splanchnic nerves cause a more or less continuous renal ischemia. If this theory is correct, — and there is considerable evidence to support it, — splanchnicectomy, if per-

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formed before permanent changes occur in the vessel walls, should improve the renal hemodynamic state.

It has been argued that since splanchnicectomy does not lower the blood pressure when metal clamps are constricting the renal vessels in dogs, it cannot improve renal circulation in man. Such reasoning is fallacious. How could the blood flow be increased by a sympathetic denervation when a mechanical obstruction still exists? I believe that in hypertension in human beings there is a neurogenic clamp — a more or less continuous vasoconstriction — and that section of the autonomic nerves to the blood vessels removes this neurogenic clamp and prevents further abnormal constriction of the arterioles.

It has repeatedly been proved that in hypertension there is a decrease in renal blood flow, and our work, using inulin and Diodrast, has shown that after splanchnicectomy in such cases the renal blood flow has been definitely maintained despite a reduction in blood pressure.[3] This suggests an increase in renal blood flow. Work being carried on at present tends to substantiate this hypothesis. This is considered the rationale for the surgical treatment of hypertension.

Surgical Procedures

The surgical technic for the treatment of arterial hypertension differs in various clinics, chiefly in the extent of sympathetic denervation. The least extensive is the subdiaphragmatic splanchnicectomy of Adson[4] and Craig.[5] Considerably more extensive is the bilateral supradiaphragmatic splanchnicectomy that I[6] have been carrying out for the past thirteen years. A somewhat more complete denervation is that of Smithwick,[7] which really combines the two operations mentioned above. A much more extensive denervation is produced by the nearly total sympathectomy of Grimson.[8] Just which of these procedures will finally be adopted cannot at present be determined. We have carried out the bilateral supradiaphragmatic splanchnicectomy in over 1500 patients, and are not convinced that additional denervation is necessary.

The operation that we perform consists in the bilateral resection of a long segment of the greater splanchnic nerves. This excision extends from the level of the seventh dorsal vertebra downward through the diaphragm. In many cases traction on the greater splanchnic nerve before it is divided pulls the celiac ganglion up to the diaphragm, so that the excision actually extends to the celiac ganglion. In addition, the lower thoracic sympathetic ganglions — usually, the eighth, ninth, tenth, eleventh and twelfth and frequently the seventh as well — are excised. The bilateral removal of the ganglions, of course, includes the various lesser and least splanchnic nerves arising from them. There is always a dramatic and immediate drop in the blood pressure, which may rise in the course of a few hours to a normal level. Generally, the pressure fluctuates more or less widely for varying periods of weeks to months before it becomes stabilized. In a few cases the pressure remains normal from the beginning.

The bilateral procedure is carried out at one operation, and the time consumed varies from forty-five minutes to an hour and a half. The patient is not shocked by this procedure, although the blood pressure may drop remarkably. In some cases it is necessary to give Neo-Synephrin during the second half of the operation and occasionally for the first few hours thereafter. Patients are encouraged to sit up at an early date, and most of them are out of bed within a week. When the upright position is first assumed, there may be a postural hypotension. This as a rule corrects itself within a few days. Bandaging of the legs and compression of the abdomen have never been found necessary. The usual stay in the hospital is two weeks following operation. Many patients are able to resume their normal activities five or six weeks following the procedure. In fact, some return to their regular work within four weeks of the operation, but a rest period of four weeks at home is advised.

Criteria for Operation

The selection of patients for the surgical treatment of hypertension has been arrived at by the trial-and-error method. When this type of therapy was first undertaken, nothing was known regarding the possibilities or the end results. We therefore operated on patients for whom today surgery would be refused. Age is a definite factor. The highest percentage of cases with sustained worth-while lowering of blood pressure occurs in patients under thirty years of age. In this age group, favorable results were obtained in nearly 80 per cent of cases. In the older age groups, only about 50 per cent of the patients have shown worth-while continued improvement. The youngest patient operated on for hypertension was eight and the oldest sixty-one years of age. Operation is usually not recommended in patients over fifty-three. Exceptions are occasionally made — for example, relief of symptoms is almost certainly obtained irrespective of lowered blood pressure. We have therefore operated on a few patients of fifty-four to fifty-eight years of age whose symptoms were so incapacitating that relief alone justified the surgical procedure. In these cases symptomatic relief was obtained, but in many the blood pressure was not significantly affected. In one patient over sixty years old, operation was performed because of a rapid loss of vision, with extensive hemorrhages and exudates in both fundi. This patient had complete restoration of vision, which has been maintained over a postoperative period of seven years, although the blood pressure was not significantly affected.

All patients are thoroughly studied in various clinics of the hospital so that the condition of the

heart, kidneys, cerebral blood vessels, and eyes can be evaluated as accurately as possible. The blood pressure is taken in both arms and generally in one leg in the horizontal, sitting and upright positions, but for purposes of comparison with the postoperative group, only the sitting readings are considered. These are made at least three times in each arm at one examination, and during the three days of special studies repeated blood-pressure records are made. Careful eye examination, including the fundi and visual fields, is made in the ophthalmologic department. The cardiac status is determined by the electrocardiogram, orthodiagram and teleoroentgenogram. Due consideration is given, of course, to any pertinent facts in the history suggesting previous cardiac insufficiency, such as nocturnal dyspnea, severe exertional dyspnea and angina. We much prefer a negative cardiac history, since the majority of deaths five to thirteen years postoperatively have occurred in patients giving a definite preoperative history of heart complications. Cardiac decompensation is a definite contraindication to surgery. If the cardiac status improves under bed rest, digitalization and other therapeutic measures, however, operation is recommended in the majority of cases. These patients are warned that although the heart may show marked improvement following splanchnicectomy, they must continue to be careful and not overexert themselves or place additional loads on an already damaged heart muscle.

Recent evidence of a coronary occlusion is also a contraindication to surgery. We have, however, operated on many patients with a previous history of coronary occlusion when the cardiac status seemed adequate. The operative risk in such patients is not greatly increased, but the prognosis for a longer postoperative life is poorer.

Gross enlargement of the heart, although definitely increasing the operative risk, is not in itself a contraindication. Many patients with enormous enlargement of the heart have shown striking reduction in cardiac size, even to normal, following the reduction in blood pressure by splanchnicectomy.

The renal status is determined by an eighteen-hour concentration test, as well as studies of urea clearance and blood nonprotein nitrogen, and urinalysis. In addition, intravenous pyelograms are made in all cases to rule out gross abnormalities in one or both kidneys. If these are unsatisfactory, retrograde pyelograms are made. Markedly contracted kidneys, polycystic kidneys and a unilateral nonfunctioning kidney are contraindications to splanchnicectomy. Evidence of moderate damage from previous pyelonephritis is no longer considered a contraindication, since some patients with this condition have shown satisfactory improvement in the blood-pressure level. Further studies are now being carried out, but a preliminary survey fails to show any correlation between the amount of damage from pyelitis and the postoperative blood-pressure level.

Decision regarding operability never rests on the maximum water concentration and urea clearance determinations alone. These findings are usually paralleled by the height of the blood nonprotein nitrogen. A nonprotein nitrogen above 45 mg. per 100 cc. when the patient has been taking adequate amounts of fluid is a definite contraindication to splanchnicectomy. It is true that we have occasionally operated when the nonprotein nitrogen was above this level, but these patients have shown only temporary improvement, occasionally lasting for a year, or no improvement. Even a nonprotein nitrogen above 42 mg. per 100 cc. suggests permanent renal damage and gives a poorer prognosis. We prefer the nonprotein nitrogen to be below 40 mg. per 100 cc.

Severe renal complications, as evidenced by a measurable amount of albumin in the urine and red cells or occasional casts in the sediment, do not militate against a good surgical result. A significant number of patients have had gross hematuria, even to the extent of so-called "renal apoplexy"; in the majority of cases these signs of renal damage have disappeared after splanchnicectomy.

A differential diagnosis between chronic glomerulonephritis and renal disease secondary to hypertension must be made, since the former is not amenable to operation. The clinical and laboratory findings may be identical in the two diseases, and the differential diagnosis may depend on the history. Usually, in chronic glomerulonephritis, there is a history of an acute episode of nephritis, often with generalized edema and albuminuria with a normal blood pressure. In some cases only the repeated finding of albumin in the urine before hypertension is manifest makes possible the diagnosis of a primary nephritis and thus rules out splanchnicectomy. Conversely, in early hypertension, the urine is normal.

The so-called "hypertensive toxemia of pregnancy," unless there is a definite history of a preceding nephritis, is not a contraindication for splanchnicectomy. Many patients give a history of an elevated blood pressure during pregnancy with a return to normal or at least a marked reduction after delivery, only to have the pressure rise still higher in a subsequent pregnancy and remain definitely elevated after its termination. In most of these cases the hypertension has tended to progress. Some of our most brilliant results following splanchicectomy have occurred in patients in whom pregnancy appeared to be the precipitating etiologic factor.

The question of whether a splanchnicectomy should be performed on a patient with a definite history of a cerebrovascular accident cannot be answered arbitrarily. Each case must be judged individually. Certain general rules have been

adopted, however. A patient under fifty years of age who has completely recovered from one or more cerebrovascular accidents does not present an unusually high surgical risk. If other findings are favorable, we recommend operation and with a definite hope of preventing another stroke. The presence of severe brain damage, as evidenced by aphasia or hemiplegia, is certainly a contraindication to this operation.

Evidence of cerebral encephalopathy manifest by mental confusion or loss of memory presents a difficult problem in deciding for or against surgery. If the mental changes are recent, especially if they are mild, a complete return of cerebral function to a normal status may be expected following splanchnicectomy. On the other hand, if the mental confusion and loss of memory are marked and of long duration, improvement cannot be expected, and operation is not recommended. Even if the changes are mild but apparently due to small repeated cerebrovascular thromboses, I believe that operation should not be performed.

Obesity is a frequent finding in hypertensive patients but, unless extreme, cannot be considered a definite contraindication to splanchnicectomy. It does, however, place an additional load on the heart, which has perhaps already been damaged, and certainly makes the operation more difficult and the convalescence more uncomfortable. We therefore recommend a low-calorie diet and do not generally advise operation until the weight has been significantly reduced.

Malignant hypertension, provided the cardiac and renal damage is not far advanced, is, in our opinion, a definite indication for splanchnicectomy, although in some clinics it is considered a contraindication. We classify as malignant only the cases showing a definite papilledema. The funduscopic examination usually reveals hemorrhages, exudates and severe angiospasm. The blood pressure is high, especially the diastolic, and most cases show moderate to severe cardiac and renal damage. Without operation the prognosis in these cases is hopeless, a large percentage of the patients dying within the first year.

In summary, the following are our criteria for operation: a patient below fifty-four years of age; a more or less continuously elevated blood pressure, with a systolic pressure over 170 and a diastolic pressure above 105; a nonprotein nitrogen below 45 mg. and preferably below 40 mg. per 100 cc.; a well compensated heart; and a relatively normal cerebral function. Exceptions are occasionally made, especially in the older age group and in cases with a slightly higher nonprotein nitrogen. These exceptions are generally made because of incapacitating symptoms, such as excruciating headaches, or when there is evidence of an otherwise hopeless malignant hypertension.

Classification of Hypertension

The evaluation of the surgical treatment of hypertension by bilateral supradiaphragmatic splanchnicectomy involves many factors. This is due to the varied manifestations of the disease. It must be remembered that arterial hypertension is a generalized disease, all organs of the body being affected; in some patients the clinical evidence of cerebral damage predominates, in others the heart is chiefly affected, and in some impaired renal function is the chief concern. Any combination of these may occur to complicate the picture further. In addition, the eye findings may give evidence of severe hypertension without cardiac or renal injury. Symptoms are absent in some patients, but are predominant in others. For these reasons a new classification, based on the dominant finding, has been suggested,[9] as follows:

Group 1 (with early, mild hypertension). These patients are entirely asymptomatic, have normal or slightly abnormal fundi and show no evidence of cardiac, renal or cerebral involvement.

Group 2 (in which symptoms are predominant). All patients in this group complain of symptoms and have mild changes in the retinal blood vessels, but display no evidences of cardiac, renal or cerebral impairment.

Group 3 (in which organic heart disease is predominant). In each case the diagnosis of heart disease is confirmed by either a definitely abnormal electrocardiogram or a teleoroentgenogram showing cardiac enlargement, or both.

Group 4 (in which cerebrovascular disease is predominant). Each patient in this group has had one or more previous cerebral accidents.

Group 5 (in which impaired renal function is predominant). Each patient shows diminished concentrating ability and urea clearance values.

Group 6 (with malignant hypertension). These patients have severe neuroretinitis, with a papilledema of 1 diopter or more, and display a rapidly progressive, downhill course.

Results of Operation

The majority of our patients have been studied at postoperative periods ranging from one to twelve years. We do not believe that earlier studies have valuable significance.

Symptomatic relief has been striking. Excruciating headaches, usually suboccipital, marked nervousness and irritability, insomnia and distressing palpitation have been greatly relieved or completely eradicated in 86 per cent of the patients still living. This percentage of improvement has persisted almost unchanged over postoperative periods of five to twelve years. Such symptomatic relief is not necessarily dependent on a significant lowering of the blood pressure or improvement in cardiac or renal function.

The blood pressure, both systolic and diastolic, was significantly reduced five to twelve years after splanchnicectomy in 81.3 per cent of the patients still living. There had been no change from preoperative levels in 12.7 per cent. Over the course of years only 6 per cent had an increase in blood pressure. Many of the patients who died (49 per cent had malignant hypertension) during the postoperative period of five to twelve years had had significant reductions in their blood pressure, but regardless of the addition of these cases to those not showing improvement, there was a worth-while reduction of blood pressure in 46.7 per cent of the entire series.

We consider a blood pressure of 140 systolic, 90 diastolic, normal for patients under forty, and one of 150 systolic, 95 diastolic, normal for those over forty. With these criteria, 20.3 per cent of patients have maintained normal pressure for five to twelve years.

A reduction in blood pressure of over 80 systolic, 25 diastolic, although not to normal, is considered a marked improvement. Such a reduction was maintained for the entire postoperative period of five to twelve years in 26 per cent of cases. A significant improvement (a reduction of more than 40 systolic, 15 diastolic) was maintained in 35 per cent.

Considering the patients whose blood pressure has been reduced to normal and those with marked and significant reductions, there was an over-all improvement in blood pressure in 81.3 per cent of the living patients, and the improvement has been maintained to date, that is, five to twelve years after operation.

The funduscopic findings in cases that before operation showed angiospastic retinitis with or without hemorrhages or exudates now show absence of angiospasm, hemorrhages or exudates in 82 per cent. Papilledema disappeared, and in the 21 patients with malignant hypertension who are still living five to twelve years after splanchnicectomy it has not returned.

The cardiac status showed a similar improvement, which was maintained over the long period of postoperative study; patients with marked enlargement of the heart preoperatively showed a significant reduction in 52 per cent. Symptomatic improvement, evidenced by relief of anginal pain, palpitation and shortness of breath, was striking. Some patients who had had frequent attacks of angina pectoris had been completely relieved, and there had been no return of painful attacks under either excitement or exercise for the several years of postoperative study. In a significant number of patients with abnormal electrocardiograms before operation, including those with angina pectoris, the electrocardiogram returned to normal.

The renal function following splanchnicectomy has shown definite improvement, both in water-concentrating ability and urea clearance. Recent studies have not been completed, but in an earlier study, 45 per cent showed a return of urea clearance to normal and 44 per cent had improvement in water concentration. Red cells and albumin have disappeared from the urinary sediment.

It should be borne in mind that practically all our hypertensive patients had had modern medical treatment, sometimes for years and under the direction of able internists, before being referred to us for splanchnicectomy. Such medical treatment had failed to prevent further progress of the disease, as evidenced by persistent or increasing blood pressure, continuing of impairment of cardiac or renal functions, advancing eye changes, cerebral accidents and intensified symptoms. Therefore, the improvement noted after splanchnicectomy can be directly attributed to the operation.

Improvement in life expectancy is best judged by the results in cases of malignant hypertension. In the series of Keith, Wagener and Barker[10] there was a mortality of 78 per cent at the end of the first year, compared to our mortality of 36 per cent after splanchnicectomy. At the end of two years under medical treatment there was a mortality of 88 per cent, compared to a mortality of 50 per cent in those treated surgically. At the end of five years only 1 of 146 patients treated medically was still living, whereas 35 per cent were living after splanchnicectomy. Of special significance is the fact that 19 per cent of our patients with preoperative malignant hypertension are still living five to thirteen years after bilateral supradiaphragmatic splanchnicectomy.

The ability to resume a gainful occupation is of vital importance to a large number of incapacitated hypertensive patients. The frequently given advice to "slow down" and "lessen or stop working" is economically impossible for a vast number of patients. Often this advice is coupled with the phrase "stop worrying." Just how a man who needs to support his family and is told that he must stop work can help from worrying is not explained. The ability of the hypertensive patient to resume work after splanchnicectomy is one of the most gratifying results. In one of our special follow-up studies extending for a postoperative period of seven years, 55.5 per cent of patients had completely recovered from their incapacitation and had been able to return to their former occupations. Many others were so improved that they were again employed, making a total improvement from incapacitation of 81.3 per cent. The majority were able to resume work only a few weeks after the bilateral supradiaphragmatic splanchnicectomy.

Perhaps as severe a test of the efficacy of splanchnicectomy for hypertension as can be made is that of pregnancy some time after the operation. Pregnancy often appears to be the instigating factor in the development of hypertension in apparently healthy women. It is well known that pregnancy frequently accelerates the hypertensive process when

the disease is already present, so much so in some cases that a therapeutic abortion is indicated to save the mother. We have a number of patients who had had severe hypertension; in one with a systolic pressure of over 300 in whom following a bilateral supradiaphragmatic splanchnicectomy the pressure dropped to and remained normal, a subsequent pregnancy was carried to completion without incident. These pregnancies occurred one to several years after the splanchnicectomy. In none did the blood pressure rise above normal either during or after the pregnancy. All patients were free of hypertensive symptoms, and none showed any evidence of cardiac impairment or abnormal renal function.

The following case reports are given to illustrate the results obtained by bilateral supradiaphragmatic splanchnicectomy in many patients with severe hypertension. The first is a case of typical malignant hypertension, the second a case of hypertension with severe angina; and the third a case of pregnancy following splanchnicectomy.

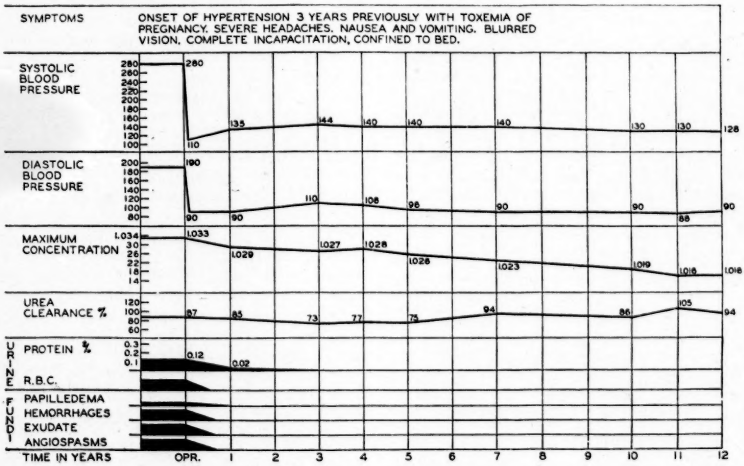
SYMPTOMS
ONSET OF HYPERTENSION 3 YEARS PREVIOUSLY WITH TOXEMIA OF PREGNANCY. SEVERE HEADACHES. NAUSEA AND VOMITING. BLURRED VISION. COMPLETE INCAPACITATION, CONFINED TO BED.
SYSTOLIC BLOOD PRESSURE
280 260 240 220 200 180 160 140 120 100
280 135 144 140 140 140 130 130 128
110
DIASTOLIC BLOOD PRESSURE
200 180 160 140 120 100 80
190 110 108 98 90 90 88 90
90 90
MAXIMUM CONCENTRATION
1.034 30 26 22 18 14
1.033 1.029 1.027 1.028 1.028 1.023 1.019 1.018 1.018
UREA CLEARANCE %
120 100 80 60
87 85 73 77 75 94 86 105 94
URINE
PROTEIN %
0.3 0.2 0.1
0.12 0.02
R.B.C.
FUNDI
PAPILLEDEMA
HEMORRHAGES
EXUDATE
ANGIOSPASMS
TIME IN YEARS
OPR. 1 2 3 4 5 6 7 8 9 10 11 12

FIGURE 1. *Summary of Data in Case 1.*

CASE 1 (Fig. 1). *Malignant hypertension.* V. E., a 22-year-old married woman, entered the hospital on June 16, 1934, complaining of severe headaches. An elevated blood pressure had been discovered during her first pregnancy 3 years previously, when she had complained of swollen ankles, unbearable headaches and blurred vision. The systolic blood pressure reached 250 with the toxemia of pregnancy; labor was induced during the 8th month, and a living infant was obtained. One year later the child died, and the patient immediately began to have episodes of severe precordial pain with associated numbness in the left arm. The headaches returned with incapacitating severity, and nausea and vomiting were associated. She had noted blurring of vision for 1 month. She had been confined to bed for the previous 8 months because of the severity of the symptoms.

Physical examination revealed a severe neuroretinitis with early papilledema, flame-shaped hemorrhages and cotton-wool patches; the retinal arteries showed marked variation in caliber, with localized angiospasms and arteriovenous compression. Both lung fields were clear. The heart was not enlarged. A soft systolic murmur was heard over the precordium. Neither kidney was palpated. There was no peripheral edema. The blood pressure averaged 280/190 in both arms.

An electrocardiogram showed inverted T waves in Leads 2 and 3. Urinalysis revealed a proteinuria of 0.12 per cent, and a moderate number of red cells and casts in the sediment. The maximum specific gravity on a 38-hour concentration test was 1.033. Urea clearance was 87 per cent. A phenolsulfonephthalein test showed 24 per cent excretion of the dye in 15 minutes. There was no anemia, and the blood serologic findings were negative.

A bilateral supradiaphragmatic splanchnicectomy was performed on June 22. The postoperative course was uneventful, and the patient was discharged in 14 days.

Follow-up study 2 months after operation disclosed a blood pressure of 145/90. The patient was completely asymptomatic. The maximum specific gravity was 1.028. The phenolsulfonephthalein test showed 30 per cent excretion of the dye in 15 minutes. The proteinuria was 0.02 per cent. Examination of the fundus revealed that the hemorrhages and exudates had completely disappeared and that the arteries were practically normal; both optic disks were well outlined.

One year after operation ti blood pressure was 135/90, and the patient was still completely asymptomatic. The ocular fundi were normal. The maximum specific gravity was 1.029, and the urea clearance was 85 per cent. The phenolsulfonephthalein test showed 37 per cent excretion of the dye in 15 minutes. There was a proteinuria of 0.02 per cent.

Three years after operation the blood pressure was 144/110. The patient complained of a recurrence of the episodes of pre-

cordial pain. An electrocardiogram showed inverted T waves in Leads 2 and 3. A left superior cervical ganglionectomy was performed. The ocular fundi were normal. There was no proteinuria. The maximum specific gravity was 1.027, and the urea clearance was 73 per cent.

A year later the blood pressure was 140/106, and the patient was asymptomatic, with normal fundi. The specific gravity was 1.028, and the urea clearance was 77 per cent. There was no proteinuria.

Five years after operation the blood pressure was 140/96. The patient was still asymptomatic, with normal fundi. An electrocardiogram was within normal limits, with upright T waves. A teleoroentgenogram revealed the heart to be of normal size. The specific gravity was 1.026, and the urea clearance was 75 per cent. There was no proteinuria.

Two years later examination revealed that the blood pressure was still 140/90; the patient was asymptomatic. There was a slight sclerosis of the retinal arterioles. There was no proteinuria. The maximum specific gravity on an 18-hour concentration test was 1.023 (previous follow-up tests had all been performed on a concentration of 36 hours). The urea clearance was 94 per cent.

Ten years after operation the blood pressure was 130/90, and the patient was asymptomatic. An electrocardiogram was normal, and the heart size was unchanged on a teleoroentgenogram. The ocular fundi showed a slight sclerosis of the arterioles. The maximum specific gravity on an 18-hour concentration test was 1.019. The urea clearance was 86 per cent.

Eleven years after operation the blood pressure was 130/88, and the patient had no symptoms. There was a slight sclerosis of the retinal arterioles. An electrocardiogram was normal, as was the heart size. The maximum specific gravity on an 18-hour concentration test was 1.016, and the urea clearance was 105 per cent.

Twelve years after operation the blood pressure was 128/90, and the patient was still asymptomatic. There was a mild sclerosis of the retinal arterioles. An electrocardiogram and the heart size were normal. The maximum specific gravity was 1.016 on an 18-hour concentration test. The urea clearance was 94 per cent.

CASE 2. *Hypertension with severe angina pectoris.* M. S., a 40-year-old housewife, entered the hospital on September 2, 1941, complaining of episodes of excruciating pain across the upper anterior chest that were consistently related to exertion and disappeared after 5 to 15 minutes of rest. She had first been discovered to have high blood pressure 10 years previously. She had had two to six episodes of severe substernal pain daily for the previous month.

Physical examination revealed a moderate sclerosis, localized angiospasms and arteriovenous nicking but no hemorrhages or papilledema. Both lung fields were clear. The heart was not enlarged; a definite presystolic gallop was heard at the apex; the aortic second sound was snapping. Neither kidney was palpated. There was no peripheral edema. The blood pressure averaged 230/150 in both arms.

An electrocardiogram revealed deeply inverted T waves in Leads 1 and 2 and in the chest leads, suggesting a recent anterior myocardial infarction. The heart size was normal on a teleoroentgenogram. Urinalysis was negative. The maximum specific gravity was 1.021. The urea clearance was 68 per cent. The blood nonprotein nitrogen was 32 mg. per 100 cc.

The patient continued to have at least two anginal seizures daily while at rest in bed. On September 9 the T waves were much less inverted than those in the previous electrocardiogram. The blood pressure remained at 220/140. On September 18, a protracted episode of severe substernal pain required morphine for relief. On the next day the electrocardiogram showed prominent Q waves in Leads 2 and 3 and evidences of a fresh posterior myocardial infarction. Anginal seizures continued while the patient was at rest in bed. Serial electrocardiograms showed evidences of healing of the infarct. The blood pressure remained high.

Because of the persistent anginal seizures and high blood pressure, bilateral splanchnicectomy was performed on October 17. Although two recent myocardial infarcts had occurred, the postoperative course was uneventful. The patient was discharged on November 5; she did not have a single anginal seizure following operation.

Follow-up examination 5 years after operation disclosed complete relief from the anginal seizures; there had been no subsequent coronary occlusion. The blood pressure was 164/114. No gallop rhythm was apparent. An electrocardiogram showed prominent Q waves in Leads 2 and 3. The heart size was normal on a teleoroentgenogram. The maximum specific gravity of the urine was 1.021.

CASE 3. *Pregnancy following splanchnicectomy.* G. T., a 23-year-old woman, was admitted to the hospital on April 16, 1938. She had first learned that she had an elevated blood pressure 2 years previously, when she had consulted a physician because of occipital headaches. The headaches increased in severity and frequency until admission. There were no other complaints.

Physical examination revealed marked attenuation of the retinal arterioles and occasional localized angiospasms; there was a cotton-wool patch temporal to the disk of the left eye; both disks were well outlined. Both lung fields were entirely clear, and the heart showed nothing unusual. Neither kidney was palpated, and there was no peripheral edema. The blood pressure averaged 230/145 in both arms.

An electrocardiogram was within normal limits. A teleoroentgenogram revealed a heart of normal size. Urinalysis was negative for proteinuria. The blood nonprotein nitrogen was 17.2 mg. per 100 cc. The maximum specific gravity on a 38-hour concentration test was 1.023. The urea clearance was 89 per cent of normal. There was no anemia, and the blood serologic findings were negative.

Bilateral splanchnicectomy was performed on April 20. The patient was discharged on the 12th postoperative day.

Follow-up examination 2 years after operation revealed complete relief from preoperative headaches; the patient was working full time as a bookkeeper and had no complaints. The ocular fundi were normal. The blood pressure was 126/82. An electrocardiogram was within normal limits, and the heart was normal on a teleoroentgenogram. The maximum specific gravity was normal at 1.026 on an 18-hour concentration test. The urea clearance was 93 per cent.

Five years after operation the patient completed a full-term pregnancy, a normal infant being delivered. The blood pressure remained normal, and there was no albuminuria during the entire pregnancy.

Seven years after operation the blood pressure was 118/86, and the patient was completely asymptomatic. An electrocardiogram was normal, and the heart size normal on a teleoroentgenogram. The maximum specific gravity was 1.025.

SUMMARY

The etiology of hypertension is considered, especially in its bearing on surgical treatment. A new classification of arterial hypertension is presented, based on the predominant pathologic lesion.

Bilateral supradiaphragmatic splanchnicectomy, which includes excision of the greater, lesser and least splanchnic nerves, is considered the procedure of choice. The operation has been performed at the University of Michigan Hospital on over 1500 patients. The results of studies over a postoperative period of one to twelve years are given. Significant improvement in reduction of blood pressure, improvement in ocular, renal and cardiac status, alleviation of symptoms, relief of incapacitation and probable prolongation of life are reported.

Three typical case reports or the relief afforded by bilateral splanchnicectomy are presented.

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PENICILLIN IN THE TREATMENT OF GONORRHEA IN WOMEN

Results of Treatment as Reported by Twelve Co-operating Venereal-Disease Clinics in Massachusetts during 1945

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THE application of penicillin seems to be the outstanding advance to date in the therapy of gonorrhea, the most frequent of all venereal infections. The results of treatment in both sexes, with or without complications, are so striking that all other forms of therapy now seem antiquated. This is not to say, however, that penicillin is a "miracle drug" that relieves the physician and follow-up workers of any further responsibility once a patient has received a course of treatment.

Critical analysis of the data available shows that one may come to some tentative conclusions. There are enough failures of treatment to necessitate careful repeated follow-up examinations, which should include at least four or five cultures and smears for the gonococcus. The optimum treatment schedule has yet to be worked out, but the underlying principles seem to aim at producing penicillin blood levels high enough to accomplish the desired results over a relatively short period rather than lower blood levels for a prolonged period. The rationale of this is twofold: the goal is to develop an ambulatory treatment that can be completed at one clinic session; and experience seems to show that dosage schedules that achieve these high penicillin blood levels produce a larger percentage of satisfactory results. Because of the well known repressive action of the drug on the spirochetes of syphilis, blood serologic tests should be taken six weeks after treatment and should be repeated in three months.

This paper represents an analysis of the data collected from twelve clinics that co-operate with the Division of Venereal Diseases, Massachusetts Department of Public Health. The study includes female patients with gonorrhea who were treated with aqueous solutions of sodium penicillin and whose cases were reported to the division on special "Penicillin Study" forms from September, 1944, to January, 1946.

Many of the numerous papers written on the use of penicillin in the treatment of gonorrhea have been reports of the results of research in this field. The data of one of the co-operating clinics in Massachusetts, which is engaged in active research, are not included in this study. We are interested in examining the results of various treatment schedules as applied by a representative group of clinicians under widely differing circumstances. It is as a picture of what penicillin may be expected to accomplish in a representative cross section of venereal-disease clinics that this paper is presented. Studies of this kind will eventually establish a sound rationale for routine treatment schedules that are applicable on a large scale for the therapy of gonorrhea in women.

TABLE 1. *Results of Penicillin Treatment of Gonorrhea in Women.*

TOTAL DOSAGE OF PENICILLIN	TOTAL NO. OF CASES	CURES		FAILURES	
		NO. OF CASES	PERCENTAGE	NO. OF CASES	PERCENTAGE
units					
100,000	135	119	88	16	12
150,000	41	41	100	0	0
200,000	44	40	91	4	9
300,000 or more	14	12	86	2	14
Totals	234	212		22	
Averages			91		9

Table 1 presents a summary of the results of treatment under the various dosage schedules employed in this series. Thirty-two cases reported on the study sheets were not followed after treatment and are not included in the table. Two hundred and thirty-four courses of treatment were given to

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200 patients with either proved or suspected gonorrhea. Those treated on suspicion without any particular clinical or laboratory evidence of gonorrhea were women who had been named as sources of infection by men with gonorrhea; in most cases these were military contacts.

The largest group of patients in the series received 100,000 units of penicillin. In all but 6 of these patients, who were treated according to the schedule of 20,000 units every two hours for five injections, the results were satisfactory, a percentage of 90 (Table 2). When penicillin first became available for distribution to the co-operating clinics, this was the schedule recommended.

Forty-one patients were treated with 150,000 units of penicillin. All of these were given 50,000 units every two hours for three doses. The results were 100 per cent satisfactory. This schedule seemed to give the best results, which is surprising in view of the fact that the 44 cases treated with 200,000 units showed failures in 4, a rate of 9 per cent.

Table 3 presents the details of the various treatment schedules employed with a total dosage of 200,000 units. Eight patients were given three injections of 66,666 units each at two-hour intervals. All were cured. This standard schedule was introduced by the Department of Public Health during the latter part of 1945. The excellent results in the small group recorded sustain the judgment in recommending the change, although the group is too small as yet to have statistical significance.

Further study of Table 3 shows that there were 4 cases of failure among patients receiving 200,000 units. One of these patients received two injections of 100,000 units each, four hours apart. Analysis of this case report disclosed that the patient was treated on suspicion on June 14, 1945. On follow-up study on June 20 and July 11 smears and cultures were negative. On August 8, two months after treatment, there was a positive culture, probably owing to reinfection rather than to failure of treatment. The patient was again treated with a course of 100,000 units (20,000 units every two hours for five doses), but the culture remained positive. A third course of 50,000 units every two hours for three injections finally resulted in a cure.

There were three failures in the group of 19 patients who received 50,000 units every two hours for four injections — a total dose of 200,000 units. Analysis of the individual case reports shows that two of these failures occurred in a patient who either was resistant to penicillin or became reinfected repeatedly, or both; the failures occurred on the second and third courses of treatment. The former may well have been caused by reinfection following the first course of treatment with 100,000 units. The patient eventually developed pelvic inflammatory disease and received a fourth course of treatment, totaling 600,000 units, in the hospital. Subsequently, four consecutive smears and cultures were negative. Two months after treatment she returned to the clinic with positive smears and cultures. Although she denied re-exposure, it is difficult to accept this case as one of failure in the fourth course of treatment. The third treatment failure occurred in a woman who returned with pelvic inflammatory disease a month after the course of therapy. There is nothing in the report to indicate that this case could not have been the result of reinfection rather than a failure of treatment.

TABLE 2. *Results of Treatment with 100,000 Units of Penicillin according to Interval between Injections.*

No. of Injections	Two Hours between Injections		Three Hours between Injections		Four Hours between Injections		Totals	
	Cures	Failures	Cures	Failures	Cures	Failures	Cures	Failures
3	3 (75%)	1 (25%)	—	1 (100%)	2 (67%)	1 (33%)	5 (62%)	3 (37%)
4	1 (100%)	—	—	—	—	—	1 (100%)	—
5	112 (90%)	13 (10%)	1 (100%)	—	—	—	113 (90%)	13 (10%)
Totals	116 (89%)	14 (11%)	1 (50%)	1 (50%)	2 (67%)	1 (33%)	119 (88%)	16 (12%)

TABLE 3. *Results of Treatment with 200,000 Units of Penicillin according to Interval between Injections.*

No. of Injections	Two Hours between Injections		Three Hours between Injections		Four Hours between Injections		Totals	
	Cures	Failures	Cures	Failures	Cures	Failures	Cures	Failures
2	—	—	—	—	7 (88%)	1 (12%)	7 (87%)	1 (12%)
3	8 (100%)	—	—	—	—	—	8 (100%)	—
4	16 (84%)	3 (16%)	—	—	—	—	16 (84%)	3 (16%)
5	4 (100%)	—	—	—	—	—	4 (100%)	—
More than 6	1 (100%)	—	4 (100%)	—	—	—	5 (100%)	—
Totals	29 (91%)	3 (9%)	4 (100%)	—	7 (88%)	1 (12%)	40 (91%)	4 (9%)

A total of 14 patients received 300,000 units or more, with failure in 2 (Table 4), one of which was the doubtful failure mentioned above. The results in this small group were 86 per cent successful. If the doubtful failure is reclassified as a case of reinfection, the rate of cure becomes 93 per cent.

Table 5 presents the results of treatment in relation to the number of courses for each patient and to the total dosage used. The first course of treatment gave satisfactory results in 93 per cent of cases regardless of the total dosage used. The patients receiving 100,000 units made the poorest showing, with cure in only 89 per cent. If the doubtful failure referred to above is regarded as a case of reinfection, the treatment in the groups in which 150,000 units or more were employed was 99 per cent successful.

The conclusion may be drawn from this series that 100,000 units of penicillin does not constitute an adequate dose for achieving uniformly reliable results in the treatment of gonorrhea in women. Any dosage schedule employing 150,000 units or more appears to be adequate except for the unusual case caused by a resistant strain.

Table 6 demonstrates a definite decline in the trend of curability as the duration of infection lengthens. Twenty-five patients with infections lasting up to fourteen days were cured; patients whose infection had persisted for fifteen to twenty-eight days showed 97 per cent cures. In the chronic cases and those in which the duration of infection was unknown, the cures were 92 and 85 per cent respectively. Recent work on the mode of action of penicillin indicates that bacteria are most vulnerable to the action of penicillin during the period of greatest reproductive activity. This may explain the difference in the response of acute gonorrhea to penicillin therapy as compared with that of the chronic condition. In addition, the greater activity of the host tissues in the characteristic reaction of an acute inflammation must be considered.

Table 7 presents the interesting observation that the percentage of cured cases was higher in the group with complications than in that without complications. The difference, however, is not statistically significant. In general, the patients with

TABLE 4. *Results of Treatment with 300,000 or More Units of Penicillin according to Interval between Injections.*

No. of Injections	Two Hours between Injections		Three Hours between Injections		Totals	
	Cures	Failures	Cures	Failures	Cures	Failures
4	2 (100%)	—	—	—	2 (100%)	—
More than 6	6 (86%)	1 (14%)	4 (80%)	1 (20%)	10 (83%)	2 (17%)
Totals	8 (89%)	1 (11%)	4 (80%)	1 (20%)	12 (86%)	2 (14%)

TABLE 5. *Results of Treatment according to Total Dosage and Courses of Penicillin.*

Total Dosage	First Course		Second Course		Third Course		Fourth Course		Totals	
	Cures	Failures	Cures	Failures	Cures	Failures	Cures	Failures	Cures	Failures
units										
100,000	110 (89%)	13 (11%)	7 (70%)	3 (30%)	2 (100%)	—	—	—	119 (88%)	16 (12%)
150,000	35 (100%)	—	5 (100%)	—	1 (100%)	—	—	—	41 (100%)	—
200,000	35 (97%)	1 (3%)	4 (67%)	2 (33%)	1 (50%)	1 (50%)	—	—	40 (91%)	4 (9%)
300,000 or more	6 (100%)	—	—	1 (100%)	5 (100%)	—	1 (50%)	1 (50%)	12 (86%)	2 (14%)
Totals	186 (93%)	14 (7%)	16 (73%)	6 (27%)	9 (90%)	1 (10%)	1 (50%)	1 (50%)	212 (91%)	22 (9%)

TABLE 6. *Results of Treatment according to Duration of Infection.*

Duration of Injection	Cures	Failures
days		
0–14	25 (100%)	—
15–28	30 (97%)	1 (3%)
29 or more	76 (92%)	7 (8%)
Unknown	81 (85%)	14 (15%)
Totals	212 (91%)	22 (9%)

TABLE 7. *Results of Treatment according to Complications.*

Type of Gonorrhea	Result	
	Cures	Failures
Uncomplicated	199 (91%)	21 (9%)
Complicated	13 (93%)	1 (7%)
Totals	212 (91%)	22 (9%)

complications received larger doses than those with uncomplicated gonorrhea. Table 7 shows, however, that penicillin is equally effective in the treatment of gonorrhea with or without complications.

* * *

This study was based on the tabulation of information sent in by twelve co-operating clinics in Massachusetts regarding cases of gonorrhea in women who had been treated with varying courses of intramuscular injections of an aqueous solution of penicillin. Two hundred and thirty-four courses of treatment were given in 200 cases. The best results were obtained by the use of 150,000 units or more of penicillin divided into three equal doses spaced two hours apart.

15 Ashburton Place

MEDICAL PROGRESS

SYPHILIS (Concluded)

G. MARSHALL CRAWFORD, M.D.*

BOSTON

REACTIONS TO TREATMENT

A word of caution has been given by Leifer[56] regarding the continuance of arsenotherapy in patients experiencing the reaction known as erythema of the ninth day. This is an entirely distinct disturbance from the systemic Herxheimer reaction, which occurs only after the initial dose of arsenic or, rarely, after the second injection. Erythema of the ninth day may occur any time within the first three weeks of arsenotherapy, and Leifer considers it a probable manifestation of sensitivity to arsenic. An erythematous eruption may or may not be present, but fever always occurs and there may be acute hepatitis. It was often assumed that arsenotherapy could safely be resumed from one to six months after erythema of the ninth day, depending on the severity of the reaction. Leifer reports 14 cases in which the reinstitution of arsenical treatment after erythema of the ninth day was followed by a severe parenchymatous injury in the form of jaundice and agranulocytosis, with or without nephritis. Arsenotherapy had been rather promptly resumed in all these patients, 12 of whom subsequently received an intensive course of penicillin without untoward reactions.

For a considerable period after the introduction of oxophenarsine hydrochloride (Mapharsen), it was maintained that the drug caused no serious reactions and comparatively few untoward effects of any kind. As it was more widely used, however, reports of damaging effects gradually appeared in the literature. Two more cases of acute agranulocytosis, one with coexisting toxic hepatitis, have been attributed to Mapharsen therapy for syphilis.[57] Colloidoclastic shock has rarely been reported from the use of Mapharsen, but another report of a case of this reaction has appeared.[58]

It has often been pointed out that post-arsphenamine jaundice is clinically indistinguishable from infectious hepatitis. A particularly interesting example of this problem was reported in a clinical observation of syphilitic patients treated in England during the period 1941–1944.[59] Fifty per cent of the patients studied developed jaundice, the majority on about the hundredth day after the first injection. Following routine sterilization of syringes before and after each injection, the incidence of hepatitis was reduced from 50 to 10 per cent. This indicates that post-arsphenamine jaundice was spread by contaminated syringes. It could just as easily be deducted that all the patients had infectious hepatitis of the epidemic type that was transmitted by the syringes.

An example of the dangers of massive drip arsenotherapy may be found in the report of 2 additional cases of encephalopathy.[60] The first patient received 240 mg. of Mapharsen over a period of eight hours; none was given thereafter. Hepatitis and toxic encephalopathy followed. The patient died eight days later. The other patient received a total dosage of 720 mg. of Mapharsen in three days. A toxic erythema developed, followed by stupor and convulsive seizures. Death occurred four days after the termination of arsenotherapy. In both cases excellent care and the best forms of treatment were used.

A systemic treatment for arsenic poisoning has appeared under the name BAL or British antilewisite (2,3-dimercaptopropanol). This compound was developed during the war as an antidote to arsenical blister gases. The compound was subse-

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quently found to be effective also in the systemic treatment of severe arsenic poisoning. Eagle[61] reported that BAL has been used in more than 200 cases in various types of arsenic poisoning with results indicating that the danger of some complications may be markedly reduced by its early administration in adequate dosage. Urinary excretion of arsenic is increased for two to four hours after therapy. The drug is injected intramuscularly in oil, 2.5 mg. per kilogram of body weight being given at each dose. Four doses are given the first two days and decreasing amounts thereafter for twelve days. In grave complications larger amounts may be used for longer periods. Of 55 patients with hemorrhagic encephalitis, 44 recovered in one to seven days. Among 51 patients with exfoliative arsenical dermatitis, 80 per cent improved within three days and recovered almost completely in thirteen days. Ten of 11 patients with agranulocytosis showed approximately normal white-cell counts within seven days. Aplastic anemia was not affected. Post-arsphenamine jaundice was cured in only 5 of 14 patients. Gluteal abscesses or cellulitis may occur with the use of this drug.

Penicillin

During the past year the use of penicillin in the treatment of syphilis has been widely extended. It should be emphasized at the outset, however, that the use of this drug in the treatment of syphilis should still be regarded as experimental and that the drug should not be employed without some routine chemotherapy, in conjunction with and subsequent to the penicillin. As pointed out below, the effectiveness of penicillin for the treatment of syphilis seems to be distinctly reduced, and increased dosage schedules have been advocated. This situation is being remedied, but it serves to illustrate how much has yet to be learned about the drug.

Experimental Research

The distribution of penicillin in the body after injection is not too difficult to determine in animals, but the fate of the drug is not entirely understood.[62] It has been shown that penicillin is widely distributed through all the tissues and organs, with the exception of the nervous system. The rate of disappearance of penicillin from the blood does not seem to be influenced by biliary obstruction in rabbits, but its effect was greatly prolonged by renal obstruction. Although the major part of administered penicillin is lost in the urine and a lesser amount in bile and saliva, there remains a portion for which the fate remains unknown.

In vitro studies have shown that the action of penicillin is far greater on organisms undergoing rapid rate of growth and with increasing temperature.[63] At high temperatures the drug kills organisms that are not undergoing growth; this action would otherwise require excessively high concentrations of the drug. Heightened effectiveness under increased temperatures explains the valuable effect of penicillin combined with hyperpyrexia in the treatment of neurosyphilis, as pointed out by clinical reports cited below.

Several variants of penicillin have been isolated in crystalline form. The comparative sensitivity of numerous bacterial strains to the different types of penicillin has been worked out.[64] Penicillin G is the one that seems to have the greatest effect on *T. pallidum*,[65] as demonstrated by the accelerated disappearance of surface organisms from dark-field-positive lesions. The proportions of penicillin fractions included in various commercial penicillins vary. All are apparently effective in the treatment of gonorrhea, and each of the various fractions appears to have enough effect on *T. pallidum* to mask syphilis when used in the treatment of gonorrhea.

It is believed that the action of penicillin interferes with bacterial metabolism in the early stages of growth.[66] Spirochetes isolated from patients receiving penicillin treatment were observed to become elongated. After being repeatedly passed through mediums containing penicillin, a laboratory strain of *T. pallidum* did not appear to have developed an increased tolerance to the drug.[67] Elongation of the spirochete was observed with electron-microscope studies of these cultures, and the organisms had also lost their flagella. This lengthening of the organism seemed to indicate an inhibition of cellular division. Although spirochetes have been repeatedly demonstrated to become resistant to arsenicals if therapy is not correctly carried out, there is some question whether penicillin resistance actually occurs. It is stated that such resistance may be an inherited characteristic originating through mutation, its origin being independent of penicillin treatment.[68] If initial doses of the drug are high and it is continued vigorously until the infection has been eliminated, resistance should certainly not appear. Acquired resistance to penicillin has been produced in some organisms in vitro although the mechanism is unknown.[66] The development of penicillin resistance in man has been unimportant, but the general problem of penicillin resistance of *T. pallidum* remains unsolved. In a case report of early syphilis resistant to treatment with penicillin, 2,400,000 units were given over a period of five days.[69] The chancre did not heal, although the serologic test for syphilis became negative after several weeks. The test subsequently became positive, and secondary lesions appeared. Retreatment consisted of only 600,000 units of penicillin in conjunction with eight hours of fever therapy; the response was excellent. This seems highly questionable as actual evidence of penicillin resistance. The correct dosage and time-dose relation of penicillin therapy are not definitely established. It is known that prolongation of administration has decided advantages even with

relatively lower dosage. The short period (five days) during which treatment was given could thus be the explanation for failure in the case reported. In vivo studies suggest that the maintenance of the minimal inhibitory concentration will result in remission of the syphilitic disease.[66] The minimal effective blood serum level of penicillin is not yet established, but it has been assumed that a serum level of 0.078 units per cubic centimeter must be maintained. Relapse should be prevented by a sufficiently prolonged period of maintenance of effective serum levels of penicillin. Higher concentrations apparently serve no useful purpose. Experimental work of this type backs up clinical experience of the value of prolongation of the duration of treatment.

Methods of Administration

Attempts to provide more prolonged effective blood levels of penicillin are being continued, but no outstanding advance has been reported during the past year. Slower absorption of penicillin from the site of injection by its incorporation in oil and wax is currently undergoing wide usage. Methods of slowing the rate of excretion have not proved satisfactory for routine employment. For all acute infections of any severity and for syphilis, the oil and wax vehicle is so far considered inferior to more rapidly diffusible diluents.

The oral administration of penicillin continues to receive a good deal of attention. Four to five times the intramuscular dose must be administered orally to obtain serum levels of comparative effectiveness. It has been shown that oral therapy with penicillin is effective in gonorrhea[70] and in other infections in which low dosages of parenteral penicillin have proved adequate.[71–74] So far as is now known, it should be unmistakably stressed that the oral administration of penicillin in the treatment of syphilis has not yet been shown to be satisfactory.

The so-called "Romansky formula"[75, 76] for penicillin in beeswax and peanut oil has been shown to maintain effective blood levels of penicillin for about twenty-four hours in some patients; it continues to be excreted in the urine for approximately three days. This method of penicillin therapy is reported as adequate for most situations but not for overwhelming infections. An average dose of 300,000 units is required. Subcutaneous administration of this preparation has also been employed with satisfactory results.[77] In the treatment of syphilis several daily doses rather than a single injection seem to be required for satisfactory effect.[78] Aluminum and penicillin mixtures have also been used,[79–81] with results that deserve continued experimentation. Like the oral administration of penicillin, however, oil and wax mixtures cannot yet be recommended for use in the treatment of syphilis. No satisfactory outpatient plan of penicillin therapy for this disease has so far been established.

Penicillin in Early Syphilis

The danger of masking early syphilis during the treatment of gonorrhea with penicillin is of considerable magnitude. Since the advent of the sulfonamide drugs and penicillin, it is simpler than ever before for the general practitioner to treat gonorrhea. The symptoms of this disease may develop and the treatment may be completed with apparent cure several days before the primary lesion of syphilis normally appears. The comparatively small amount of penicillin necessary to cure gonorrhea is sufficient to abort temporarily the lesions of early syphilis for a considerable period. I have observed a case of early syphilis with a history of penicillin therapy for gonorrhea fourteen months prior to the appearance of clinical early syphilis. Exposure to venereal infection of any sort during the intervening period was consistently denied. Continued reports of this phenomenon have appeared in print, and one cannot be too careful in following patients with gonorrhea for some months after treatment.

Experimental work with small doses of penicillin comparable to those used in the treatment of gonorrhea has been carried out in rabbits inoculated with syphilis. It was the opinion of Magnuson and Eagle,[82] who did this work, that an actual abortion of the infection, rather than suppression of the development of the primary lesion, took place. Many of the delayed lesions were so small that comparable lesions in man might not be detected, an apparently asymptomatic condition being thus produced. The authors believed that patients with gonorrhea should be followed clinically and serologically for four months or longer; this certainly seems to be a minimum period of observation. A sufficient number of case reports illustrating the danger of suppressing syphilis during gonorrhea therapy[83–87] are available to indicate that this may become a public-health problem. Some authors believe that when there is evidence or suspicion of coexisting syphilis, penicillin therapy for gonorrhea should be withheld until a definite diagnosis of syphilis can be established or eliminated.

The frequency with which penicillin therapy for syphilis is accompanied by a Herxheimer reaction makes it possible to utilize this phenomenon as a possible clue to syphilis when penicillin is used in the treatment of other infections. It has been stated that the occurrence of chills or fever accompanying penicillin therapy for gonorrhea not obviously complicated by syphilis is strong presumptive evidence of the coexistence of syphilis.[88] There are exceptions to the rule, but it is at least a safe precaution to subject a patient displaying a febrile reaction to closer than usual scrutiny for a period of several months following penicillin treatment for gonorrhea.

Sufficient data are beginning to accumulate regarding the treatment of early syphilis with penicillin to establish a more adequate appraisal of the dosage required to achieve satisfactory results. Only comparatively immediate effects can be deduced, however, until the patients have been followed for periods up to at least twenty years. Pillsbury[89, 90] reports follow-up examinations of 792 patients, six months or more after treatment with penicillin as given by the routine Army schedule. Tables are presented showing the incidence of relapse, the types of lesions, the results of serologic tests at various intervals, as well as a comparison of these penicillin-treated patients with the groups receiving prolonged courses of arsenicals and heavy metal, and the twenty-day intensive arsenobismuth plans of therapy. Pillsbury found that although penicillin therapy in early syphilis exhibits few toxic effects and the patient is rendered promptly noninfectious, with a low incidence of infectious relapses, this treatment compares unfavorably with arsenobismuth therapy in its achievement and maintenance of seronegativity. With a prompt diagnosis of syphilis the effectiveness of a single course of penicillin treatment is extremely high; 98.18 per cent of seronegative primary syphilis cases and 87.32 per cent of seropositive primary syphilis cases were considered satisfactory cures. Of the patients with secondary syphilis only 72.07 per cent became seronegative. Spinal-fluid examinations showed the incidence of progression to neurosyphilis to be extremely low as compared with those following arsphenamine and heavy-metal therapy. Penicillin, as a single therapeutic agent against syphilis, although it is remarkably effective, appears to deserve the assistance of some metallic therapy. Schoch and Alexander[91] advocate the concurrent use of penicillin and Mapharsen. They have given 2,400,000 units of penicillin over a period of seven and a half days in conjunction with 40 mg. of Mapharsen daily for eight days; an alternate program includes the same amount of penicillin with bismuth salicylate 0.2 gm. in oil on alternate days for five injections. The results with both combinations show a definitely higher cure rate than with penicillin alone. These authors also advocate coincidental penicillin treatment of sexual partners, regardless of proof of infection, to prevent reinfections of the so-called "ping-pong type." Penicillin schedules employed by the United States Navy[92] require 2,400,000 units for primary syphilis, whereas patients with secondary and latent cases receive 4,000,000 units. Therapeutic results were comparable to those of the preceding reports.[93] Others are in agreement that a dosage of 2,400,000 units is the minimal satisfactory amount of penicillin for early syphilis and that varying quantities of chemotherapy in conjunction with or subsequent to the penicillin are advisable.[94–101] There has been experimental work in animals to verify this opinion.[102] The use of penicillin combined with fever therapy in the treatment of early syphilis has also been advocated.[103] Small groups of patients were treated with varying amounts of penicillin and concurrent hyperpyrexia. The results showed that smaller amounts of penicillin were necessary to cure early syphilis when administered in conjunction with fever therapy. Too little has been done with this to warrant definitive statements regarding dosage. Appraisal of these reports on the penicillin treatment of early syphilis will clearly indicate that dosage schedules, time-dose relations and combined-therapy methods require a great deal of further study before optimal programs are worked out.

Penicillin during Pregnancy

It has been demonstrated by a number of observers that penicillin passes through the placenta in sufficient amounts to provide an adequate bacteriostatic level in the fetal circulation.[104–106] The obvious inference is that penicillin should eradicate syphilitic infections in both the mother and fetus. Since transmission to the fetus has been shown as early as the tenth week of gestation,[107] satisfactory treatment of prenatal syphilis early in pregnancy should be readily accomplished. There are clinical reports indicating that this is a safe and effective procedure. The penicillin treatment of groups of pregnant syphilitic women in Baltimore and Philadelphia clinics exhibited highly successful results in the prevention of congenital syphilis.[108, 109] It was found that reversal of the mother's blood serologic tests to negativity was not necessary to produce a normal infant. Many infants who were born with positive serologic reactions became negative within a month's time. All the mothers had early syphilis; some were treated as late as the thirty-second week in pregnancy. A reduced initial penicillin dosage for the first forty-eight hours is advocated to avoid possible reactions. The Baltimore group believes that any suggestion that penicillin has abortifacient effects is unwarranted. It is advisable to follow the pregnant woman clinically and with repeated titered serologic tests at least once a month until delivery and at appropriate intervals thereafter. Retreatment with penicillin should be given to the mother during pregnancy if there is evidence of clinical or serologic relapse or if the original maternal serologic titer does not significantly decline within three months after treatment. It is believed that, pending further information, a pregnant syphilitic woman whose infection has apparently been previously treated successfully with penicillin should be retreated with penicillin in each succeeding pregnancy.

Congenital Syphilis

Although the earliest reports regarding the penicillin treatment of congenital syphilis were not so optimistic as those in other forms of the disease, later publications are somewhat more encouraging.

The most satisfactory results have been obtained in cases of early congenital syphilis with manifest symptoms.[110, 111] In patients with asymptomatic early congenital syphilis there is no clinical guide, but a gradual decrease in the titer of the blood may be observed in most cases. In late congenital syphilis, especially among patients with interstitial keratitis and neurosyphilis, clinical and laboratory findings indicate a much poorer response.[110] The penicillin treatment of syphilis in infants and children, either the congenital or the acquired disease, leaves much to be desired.[112] Dosage schedules so far recommended vary from 20,000 units per kilogram of body weight (divided into sixty doses)[113] to as high as three times that amount.[110, 114] Periods of administration of from seven and a half to twenty days have been advocated.

Late Syphilis

The predominant attention to the use of penicillin in syphilis has been directed toward early infections. A few reports regarding management of the later stages of the disease are becoming available. A small group of patients with benign late gummatous syphilis were treated and followed for an average period of about fourteen months.[115] Cutaneous, mucocutaneous and mucous-membrane gummas, osseous lesions and hepatic gummas were included. The minimal dosage was 2,000,000 units, and the maximum was 4,000,000 units in some cases. There was a relatively rapid symptomatic response in all patients, although the objective findings in the hepatic cases were slower to improve. There was also a case of incidental gummatous keratitis that responded satisfactorily.

Syphilitic Nephrosis

One of the less frequent but more spectacular symptoms of syphilis is acute syphilitic nephrosis. The patients develop marked and widespread edema, with gross proteinuria and critically reduced plasma proteins. To establish the diagnosis, syphilis must be proved, with the absence of other urinary findings and lack of evidence of any of the usual causes of nephrosis. Two cases of rather dramatic response of acute syphilitic nephrosis to treatment with penicillin were recently reported.[116, 117]

Ocular Syphilis

Syphilis can affect the eye in many ways, and the treatment in these cases requires considerable care. The eye is an organ in which the occurrence of a Herxheimer reaction may cause extremely unfortunate destruction. In a group of 17 patients with iritis associated with the lesions of early syphilis who were treated with penicillin alone, the incidence of Herxheimer reactions was kept down by properly reduced initial dosage.[118] Treatment was started with 5000 to 20,000 units, the dosage being gradually increased to 50,000 to 60,000 units, with satisfactory beneficial effects.

Cardiovascular Syphilis

There has been considerable hesitancy on the part of cardiologists regarding the use of penicillin in cardiovascular syphilis.[119] This uncertainty is not shared by most syphilologists, although more care is exerted in the plan of treatment employed. It is a well known fact that Herxheimer reactions can be prevented by steadily increasing doses of any drug used in the treatment of syphilis. Even when initial therapy is low in dosage, a repetition of the same small amount may be followed by a Herxheimer reaction. It is quite likely that the pursuance of this policy would be accompanied by extremely few cases of reaction to penicillin in cardiovascular syphilis.

Neurosyphilis

There were for a time conflicting reports regarding the penetration of penicillin into the spinal fluid, regardless of means of administration other than intrathecal. Further reports indicate that systemic administration of penicillin in doses generally used will not consistently produce measurable levels of penicillin in the spinal fluid.[120] There is apparently a somewhat greater tendency for the drug to reach the subarachnoid space in the presence of meningitis. Therapeutic spinal-fluid levels of penicillin are not attained unless blood serum levels much higher than the usual minimal effective quotient are maintained for periods of twelve hours or more. Massive doses of penicillin by continuous intravenous drip were followed by the appearance of penicillin in significant amounts in the spinal fluid of a large percentage of patients.[121] The use of fever in conjunction with intramuscular penicillin does not appear to affect the concentration of penicillin reaching the spinal fluid.[122] The penetration of penicillin through the meninges seems to be irregular and unpredictable in meningeal infections of all types.[123]

Nevertheless, there are ample reports substantiating the value of penicillin in the treatment of various forms of neurosyphilis. Again, some of the best results have been obtained when the drug is used in conjunction with other forms of therapy. Large and small groups of cases, including all types of neurosyphilis, have shown encouraging results, except in the end stages of general paresis.[92, 124–133] Smaller amounts of penicillin and shorter courses of fever therapy have been found necessary when given concurrently or in succession than when either was used alone. The use of this combination in primary optic atrophy is quite encouraging. It is the opinion of most observers that all forms of parenchymatous neurosyphilis require fever therapy as well as penicillin. Some state that improvement with penicillin appears sooner than with other methods; it is fre-

quently manifested within a few months, rather than as long as a year or more after malaria therapy. The most striking effects of penicillin are exerted on the spinal-fluid formula, where some improvement may be noted by the time therapy is terminated. There is no correlation between spinal-fluid response and the effect on blood serologic findings. The symptomatic phases of tabes dorsalis respond to penicillin therapy to an encouraging extent, with the exception of Charcot joints. Whereas penicillin alone is apparently no better than malaria alone and probably is not so effective, the two together appear to enhance each other's effect. Dosage schedules of penicillin for neurosyphilis have varied widely, from 4,000,000 to 10,000,000 units being advocated. Some observers consider repeated courses of penicillin at intervals of a few months more beneficial, but in general the higher dosage programs with prolongation of the time of administration of a single course are preferred. There is fairly general agreement that penicillin alone is not capable of controlling the graver forms of parenchymatous neurosyphilis.

The intrathecal administration of penicillin continues to receive some attention. When introduced in this manner the drug is known to remain in the spinal fluid for periods of twenty-four to seventy-two hours. The injections are given by the Swift–Ellis technic. Treatments may be given daily or as much as a week apart; the suggested doses are at great variance.[134–136] The number of treatments that can or should be given has not yet been determined. Intrathecal penicillin may be used in cases in which malaria therapy is contraindicated, and the results are encouraging. Combined intraspinal and intramuscular penicillin has also been advocated. This method is certainly not yet adaptable for general use, since some serious reactions have occurred.

Reactions to Penicillin

In general, it may still be said that reactions to penicillin therapy have been fewer and milder than those with any form of treatment for syphilis heretofore devised. Nevertheless, as with practically every new drug of any sort, an increasing number and variety of side actions have been observed.

The Herxheimer reaction is perhaps the most frequent and is of little importance in early syphilis, but may be dangerous in several forms of visceral syphilis. This may be avoided by starting with small doses (as little as 1000 units) and gradually increasing to the optimum dose.

Urticaria has been observed rather frequently and is, as a rule, merely a troublesome affair. Angioneurotic edema is less frequent but may even prove fatal.[137] Fungous infections are not infrequently aggravated,[92, 138, 139] and the so-called "id eruptions" may appear, either epidermophytids or bacterids.[140] It is believed by some investigators that a previous acute fungous infection may cause increased reactivity to penicillin.[141–143] The tissue primarily affected in most penicillin reactions is reported to be the blood vessels rather than the epidermis. Purpuric eruptions and severe arthralgia have occurred.[139] A syndrome similar to serum sickness has been observed on a number of occasions.[141–145] Eruptions typical of toxic erythema multiforme have been described, as have those characteristic of erythema nodosum.[145] Aggravation of a considerable variety of pre-existing skin diseases has been reported.[138] Contact dermatitis is not infrequently observed,[146–157] including involvement of the eyelids. This is of the greatest significance among medical personnel and laboratory workers handling penicillin solutions over long periods.

I have observed a case of an extremely severe reaction to penicillin that nearly caused death. So far as could be ascertained from the preceding physicians, the patient had received no other drug known to be capable of causing dermatitis. After three days of penicillin therapy for an upper respiratory infection, the patient developed a toxic eruption similar to erythema multiforme. Within twenty-four hours it became generalized, and mucous-membrane lesions interfered with the taking of nourishment. On the third day there were dysphagia and nausea, indicating probable lesions of the gastrointestinal tract. Generalized edema and exfoliative dermatitis quickly followed. Six weeks of hospitalization were required for recovery.

Decreased Potency

Unfortunate publicity by the lay press gave rise to doubts in the mind of the general public and many physicians regarding the efficacy of penicillin during the past year. There were some grossly inaccurate and irresponsible statements in the newspapers before any official scientific report could be prepared and released. It became known to those most closely following penicillin research toward the middle of 1944 that the treatment of syphilis with this drug was somewhat less satisfactory. Many wheels were immediately set turning to decipher the cause, and eventually it was found that the increased purity of commercial penicillin was at fault. There are several penicillins, and penicillin K has been shown to be of little or no value in the treatment of syphilis, as well as certain other infections, because it is too rapidly destroyed in the body.[158] As commercially supplied by some manufacturers in a purer form, far larger amounts of penicillin K were included; the amount was not large enough to cause a serious reduction in the value of penicillin in the treatment of syphilis and need not have caused alarm. Progressively less penicillin K is now found in commercial preparations, and the situation has meanwhile been controlled by the mere increase of penicillin dosage in the treatment of syphilis. An official statement on the use of penicillin in syphilis was finally released

after the appearance of newspaper publicity.[159] Subsequently, a full report was published giving suggestions regarding the use of the drug in the treatment of syphilis.[160, 161]

Although the best method for the employment of penicillin in the treatment of syphilis cannot be arbitrarily stated, certain minimum suggestions for treatment were given. For seronegative primary syphilis not less than 3,600,000 units was advised, and for seropositive primary and early secondary syphilis, not less than 5,400,000 units seemed imperative. In cases of relapse, including possible reinfection, after previous treatment, the course of 5,400,000 units should be repeated, followed by 360 mg. of Mapharsen or an analogous drug given twice to three times weekly in six individual intravenous injections of 60 mg. each, in addition to 1200 mg. of bismuth subsalicylate given twice weekly in six individual intramuscular injections of 0.2 gm. each. For a second relapse of early syphilis after previous penicillin treatment the patient should be transferred from penicillin entirely and placed on intensive metal therapy. Further recommendations were given for the management of various other phases of syphilis and its complications. The administration of penicillin in oil and wax for the treatment of syphilis has not been worked out sufficiently to be considered satisfactory. Under no circumstances should penicillin in its present available form be administered orally for the treatment of syphilis. The changing character of commercial penicillin and the consequent alteration in plans of administration should serve to emphasize that penicillin therapy for syphilis is still incompletely evaluated. It will take some years of further work and careful follow-up study before the actual status of this drug in the management of syphilis can be finally determined.

Summary

The release of several million young men from military duty places a greater burden than ever on public-health facilities in the prevention of venereal disease. The responsibility is squarely back on the shoulders of every state and local board of health, although the United States Public Health Service is still carrying on large-scale control measures. Education of the public continues to be of inestimable value in this respect.

The state of Alabama is continuing its legally required mass blood-testing program with extremely satisfactory results.

Studies of mortality on a nationwide basis indicate that the death rate from syphilis is slowly but steadily decreasing. Figures indicate that untreated syphilis may reduce the span of life by as much as 20 per cent. Properly treated syphilis, however, will shorten the life expectancy only about half as much.

Serologic problems in the diagnosis of syphilis and false-positive blood tests continue to be a stumbling block. The question of reinfection of the human being with *Treponema pallidum* may have been overemphasized in the face of rapid cures by recent methods of intensive therapy and by the use of penicillin. Advocates of any form of treatment may be too reluctant to admit the likelihood of relapse.

A most instructive ten-year study of late syphilis has finally appeared, showing conclusively that adequate antisyphilitic treatment reduces the hazard of late serious complications to a minimum even though the blood serologic reactions may not reverse to negative.

A survey of a large group of patients undergoing lumbar punctures suggests that the emotional reaction of the patient may be of great importance in the incidence of post-puncture headaches.

The treatment of syphilis seems to swing ever farther away from the massive dose five-day schedules. Multiple injection programs over short periods have proved much safer. One of the most important advances in combating treatment reactions is the use of BAL (2,3-dimercaptopropanol). This drug has been found to be remarkably effective in the systemic treatment of several forms of severe arsenic poisoning. Urinary excretion of arsenic is strikingly increased, and side actions from this drug are comparatively few. Such complications as hemorrhagic encephalitis, exfoliative dermatitis, agranulocytosis and post-arsphenamine jaundice have shown most gratifying response.

The greatest emphasis in the treatment of syphilis will continue to lie in the use of penicillin. Experimental studies with the various penicillins, regarding methods of administration, effects on specific organisms, the possible development of resistance and so forth continue. As yet, the use of the highly soluble forms of penicillin, with frequent injections over periods of some days, is the only acceptable method of administration. Less frequent administration in oil and wax may prove to be suitable. The combination of penicillin with arsenotherapy and the concurrent use of penicillin with hyperpyrexia seem to hold the greatest promise. One pitfall is the possibility of masking early syphilis with the use of small amounts of penicillin for the treatment of gonorrhea; many cases have been reported. The greatest volume of penicillin therapy has been given in early syphilis, but as yet an entirely satisfactory schedule has not been worked out. Its use in other forms of the disease lags somewhat but is also encouraging. Reactions to penicillin have increased in number and variety but have rarely been grave.

Perhaps the best example of the fact that penicillin therapy for syphilis should still be considered largely experimental is the altered potency of this drug. A number of commercial preparations have been found to contain large proportions of a type of penicillin that is comparatively ineffective against syphilis. This has necessitated marked increases in

the amount of the drug necessary to provide satisfactory response. It can hardly be said that a great deal more is known about the effectiveness or long-term value of penicillin at present than a year ago. It must again be stated that much more work and many more years will elapse before satisfactory programs are established.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 33081

PRESENTATION OF CASE

A fourteen-month-old boy was brought to the hospital in a semistuporous condition.

The patient had been born in the eighth month of pregnancy after premature spontaneous rupture of the fetal membranes. The mother was well. The father, an Army veteran, had had malaria and suffered from hay fever. No difficulties attended the delivery, and the infant was subsequently well until the onset of the present illness. He talked at one year and before admission was walking with help. Three months before admission, a nystagmus was noted. One month later the appetite began to fail, and in the two months before admission there was a weight loss of 2 pounds. Immunizations against diphtheria, pertussis and tetanus were carried out during the same period. In the month before admission a habit of pounding the fists on the head was noted, but in general the child was not thought to be sick until a week before admission, when a moderate upper respiratory infection with laryngitis developed. This cleared without special treatment, and the patient was well until the day of admission. At breakfast he seemed feverish and restless. The mother administered an enema, the return being gray green. Afterward the patient screamed continuously for two hours, doubled up, closed his eyes and put back his head. The temperature was found to be elevated. He vomited four times and could not retain fluid.

Physical examination showed the skin and scleras to be faintly yellow. The head measured 47 cm., and the chest 45 cm. in circumference. There was a slight left lateral nystagmus, as well as tonic deviation of the eyes to the left. The pupils were equal and reacted to light. The fundi were normal, as were the nose and ears. Slight weakness of the right lower facial muscles was observed. The pharynx was slightly reddened. The neck resisted flexion. The heart, lungs and abdomen were normal. The patient moved all extremities freely. The limb reflexes were normal, but the abdominal reflexes were absent.

The temperature was 105°F., the pulse 190, and the respirations 34.

Examination of the blood disclosed a red-cell count of 4,200,000 and a white-cell count of 17,000, with 62 per cent neutrophils.

No urine was obtained until the second day after glucose had been given intravenously. Then only a small amount was obtained, which showed an orange sugar reaction and a +++ test for acetone. The initial lumbar puncture yielded several cubic centimeters of bloody fluid that was slightly, but definitely, xanthochromic after centrifugation. The pressure was increased, but the patient was sitting and crying. Microscopically, the fluid contained innumerable red cells, as well as 60 lymphocytes per cubic millimeter and no polymorphonuclear cells. No organisms were found. The Pandy test was strongly positive. The protein was 440 mg., and the sugar 76 mg. per 100 cc., and the chloride 126 milliequiv. per liter.

X-ray examination of the skull was negative. Abundant colonies of alpha-hemolytic streptococci were cultured from the throat. There was no growth from the spinal fluid on chocolate agar. The blood-agar plate was contaminated.

The immediate treatment consisted of intravenous fluids and intramuscular penicillin. The temperature and pulse had fallen to normal by the second day, but soon began to rise again. Only 3 drops of pink fluid under little pressure were obtained on two additional lumbar taps. The fluid contained 80,000 red cells, of which 20 per cent were crenated, and 60 lymphocytes per cubic millimeter. On the afternoon of the same day the neurologic findings were somewhat altered. The right facial weakness was absent, and the eyes were held straight, deviating only occasionally to the right and left. The plantar reflexes were extensor. The patient was restless and irritable. Three hours later he was deeply comatose, with gasping respirations at a rate of 16 per minute. The reflexes were depressed. There was an erythematous macular rash on the cheeks and trunk that did not fade on pressure. On the same evening, he stopped breathing while being prepared for operation. The air passages were suctioned, and manual oxygen insufflation through an intratracheal tube was carried out. An operation was then performed.

DIFFERENTIAL DIAGNOSIS

DR. JOST J. MICHELSEN: I think it will be agreed that there is little information in this record to help us in arriving at a satisfactory conclusion. Of course, a neurologic diagnosis in this age group is always difficult, since the history and the results of examination are, as a rule, incomplete. In the case under discussion information is even more scanty than in the average.

It is almost certain that the patient had some sort of intracranial disease. We might even go a step farther and say that there was probably increased

intracranial pressure. Apparently, there was terminal respiratory failure, which is a common occurrence in cases with increased intracranial pressure. Before I continue with the discussion, however, I should like to ask two questions, How should one interpret the erythematous macular rash on the cheeks and trunk during the terminal phase of the disease, and what is the significance of the sugar and acetone found in the urine?

DR. ALLAN M. BUTLER: I do not know the significance of the rash. I did not see it. So far as the sugar in the urine is concerned, according to the abstract the first specimen was obtained after intravenous glucose was started.

A PHYSICIAN: It was obtained after the intravenous drip had been administered for twenty-four hours.

DR. MICHELSEN: Is it usual for acetone to be present with such intravenous glucose?

DR. BUTLER: If the urine was obtained after twenty-four hours of intravenous glucose and the patient did not have diabetes, the acetonuria was unusual.

DR. MICHELSEN: Let us scrutinize the data that might help to determine the type of lesion that this patient had. We are told that there was rigidity of the neck. As is well known, rigidity of the neck is most frequent with intracranial infections, particularly with those of the subarachnoid and subdural spaces; it also occurs as a manifestation of meningeal irritation following hemorrhage into the subarachnoid and subdural spaces. Less often, it is found in association with tumors that occupy the posterior fossa or as a result of herniation of the cerebellar tonsils into the foramen magnum. There is no evidence that the patient had intracranial sepsis, notwithstanding the fact that a few days prior to the onset of the more recent manifestations there was an upper respiratory infection. Offhand, there is also no evidence that the child had a brain tumor. This leaves, as the only alternative, an intracranial hemorrhage. The cerebrospinal-fluid findings suggest that this hemorrhage occurred into either the subarachnoid space or the ventricular system, or perhaps both. The question then arises, How much significance should be attributed to the cerebrospinal-fluid findings of 80,000 red cells and 60 lymphocytes per cubic millimeter? There seems to be something wrong in this observation. Considering the high white-cell count in the blood—17,000, with 62 per cent neutrophils—and the number of red cells in the spinal fluid, one would expect about 200 polymorphonuclears in the spinal fluid. Apparently, only red cells and lymphocytes were found. The differential count could not have been correct. It is said that the fluid after the initial lumbar puncture, which contained a large number of red cells, was definitely xanthochromic after centrifugation. I should expect any grossly bloody cerebrospinal fluid to show discoloration of the supernatant fluid after centrifugation, since, of course, it is mixed with serum. I should also assume that this lumbar puncture was difficult, since a routine lumbar puncture is not performed in the sitting position. As a rule, if possible, we use three test tubes to determine the source of blood in the cerebrospinal fluid. If the cerebrospinal fluid is equally bloody in all three, we are compelled to assume that the bleeding has occurred prior to the lumbar puncture, most probably in the intracranial cavity. If, however, the appearance of the fluid changes and the second and third fluid portion look clearer and contain less blood than the first one, it is likely that the blood originated from the site of the puncture. Is there any information regarding this point in the hospital record?

A PHYSICIAN: No; only one tube was used, since the fluid came out as if under pressure.

DR. MICHELSEN: There was actually increased pressure, then.

Let us assume that an intracranial hemorrhage had occurred and discuss some of the causes of such an event. A hemorrhage may be due to trauma, a congenital aneurysm, an angiomatous tumor and disease of the cerebral arteries following infections, including bacterial endocarditis and hemorrhagic diathesis. There is nothing to indicate that this child had received a head injury or that there was a hemorrhagic diathesis. The spinal-fluid picture was hardly consistent with that of bacterial endocarditis. Furthermore, the heart was normal.

Congenital aneurysm is one of the most frequent lesions producing subarachnoid hemorrhage with symptoms of meningeal irritation, changes of awareness, fever, glycosuria and certain focal signs, such as were present in this case. I have never seen a subarachnoid hemorrhage from a congenital aneurysm in an infant, however, and I did not find any case reported in the literature. Our choice, then, seems to be limited to an angiomatous malformation or arterial disease as a result of infection. This child had an infection a week before admission. Throat cultures showed abundant alpha-hemolytic streptococci. Infections such as diphtheria, influenza, scarlet fever and pneumonia can produce destructive changes in the smooth muscle and elastic tissue of the media of the arteries, resulting in necrosis and subsequent hemorrhage. Since I have no personal experience with rare types of arterial hemorrhage, I consulted various books and found that these changes reach their maximum on the eighteenth day or later. If that observation is correct, the much shorter interval between infection and hemorrhage in the case under discussion precludes this possibility. Moreover, the onset of the disease probably antedated the upper respiratory infection by several months. Nystagmus was noted at the age of eleven months, in addition to a habit of pounding the fists against the head, presumably indicating that the child had headaches.

Was the nystagmus a manifestation of the local effect of the disease, or was it a symptom of a minor hemorrhage at that time? This question is difficult to answer. My guess is that the nystagmus was due to involvement of certain structures in the posterior fossa rather than to a minor hemorrhage. This leads us to the problem of localization of the lesion. Do the other neurologic findings point to a lesion in the posterior fossa? They are at least consistent with it. There was weakness of the right lower facial nerve, which may have been due to brain-stem disease. The bilateral Babinski signs do not help in the localization at all.

In summary, I might say that subarachnoid hemorrhage from a congenital aneurysm is quite unlikely, that I hesitate to consider the possibility of a hemorrhage as the result of postinflammatory arterial changes and that the possibility of an angioma is a fairly good one, if the blood in the cerebrospinal fluid was not due to a bloody tap. Without the cerebrospinal-fluid findings one thinks of a tumor, whose type I cannot predict. As to the localization, all the evidence given to us points to a lesion in the posterior fossa. Needless to say, I expect to be wrong on all counts.

DR. BUTLER: I am astonished that you did not ask to see the x-ray films.

DR. MICHELSEN: I did not ask because they were said to be negative.

DR. BUTLER: Do you accept that as correct?

DR. MICHELSEN: I trust the X-ray Department.

DR. BUTLER: I should like to see the films. The reason I ask is that it is hard for me to believe that there was no separation of the sutures. Do you think that there was, Dr. Schatzki?

DR. RICHARD SCHATZKI: No.

DR. BUTLER: This was a fourteen-month-old baby. You are sure that these sutures are no wider than they should be?

DR. SCHATZKI: I may be wrong, but I do not care to qualify the statement.

DR. BUTLER: The abstract of the case fails to indicate the severe state of collapse. The doctors who took care of the patient were handicapped in carrying out diagnostic and surgical procedures because they thought the child was going to die at any moment. The first neurologic note states: "He will have to be studied as rapidly as possible consistent with his condition. I agree that the extreme dehydration must be treated now." Another note by the neurosurgeon reads: "The child was taken to the operating room at 5:35 p.m., and while the head was being shaved, respirations ceased. The air passages were cleared. The child was intubated, and the above procedure was done with oxygen insufflation" — the "above procedure" being bilateral burr holes. One must be careful about performing a lumbar puncture in a patient like this. I question the advisability of doing a lumbar puncture in the sitting position, unless there is some excellent reason for doing so; the reclining position appears preferable. When a lumbar puncture is performed on a child in whom one suspects increased intracranial pressure, the fluid should be removed with the greatest of care and only the minimal amount necessary for diagnostic procedures withdrawn. If evidence of increased intracranial pressure has been obtained by burr holes, it seems to me that the pressure should be reduced by ventricular tap. If desired, ventriculograms can then be obtained. Pneumoencephalograms in such patients with increased intracranial pressure are to be avoided as unduly dangerous. In this case, however, we shall learn from the pathologist's findings that there was not much that could have been done.

DR. F. DENNETTE ADAMS: How do you account for the high white-cell count and fever?

DR. BUTLER: The patient may have had some infection. The degree of dehydration alone, however, could have accounted for the elevation of the white-cell count. The dehydration, in addition to the intracranial disease, may have caused the elevated temperature.

CLINICAL DIAGNOSIS

Subdural hematoma?

DR. MICHELSEN'S DIAGNOSIS

Expanding lesion in posterior fossa, type undetermined.

ANATOMICAL DIAGNOSIS

Brain tumor, probably oligodendroglioma.

PATHOLOGICAL DISCUSSION

DR. CHARLES S. KUBIK: I agree with Dr. Michelsen that this was an unusually difficult case. I think that he did very well with the data available.

There was a soft tumor, almost gelatinous in consistence, 6 cm. in diameter, above the optic chiasm. It extended forward along the medial portions of the orbital surfaces of the frontal lobes, backward to the interpeduncular space and upward into the hypothalamus and third ventricle. The optic chiasm, olfactory lobes, tuber cinereum, a large part of the hypothalamus and the corticospinal tracts were invaded by the tumor. I should have expected serious impairment of vision. In the upper part of the tumor there was a small hemorrhage, communicating with the third ventricle, which unquestionably was the source of the blood in the spinal fluid.

We have had several other tumors in the same locality, all of which were more solid and less discrete and were composed of slender fusiform cells, apparently derived from the infundibulum. In this case the microscopic findings were quite different, and I do not know how to classify the tumor. The cells were rounded and fairly well stained, resembling

oligodendrocytes, but the gelatinous consistence of the tumor was unlike that of oligodendroglioma.

DR. TRACY B. MALLORY: Essentially, nothing was found in the rest of the body. There was a moderate degree of atelectasis of the lung, and the bronchi contained mucinous exudate, a finding that one would expect with the degree of respiratory difficulty that this child had had during life.

CASE 33082

PRESENTATION OF CASE

A thirty-seven-year-old pregnant housewife entered the hospital in coma.

A week before admission, during the sixth month of an apparently normal pregnancy, the patient had begun to complain of headache. Two days before admission a physician found the temperature to be 102°F. Since there was evidence of an upper respiratory infection, he ordered aspirin and phenacetin that day and again on the morning before admission, when the temperature was 100°F. The headache had increased by that time, and 15 mg. of morphine was prescribed. At midnight relatives found the patient unresponsive and "stiff all over," with a temperature of 104°F. and labored breathing. The family stated that she had passed little or no urine in the preceding two days, although she had taken fluids frequently. The physician injected 300,000 units of penicillin in oil before sending her to the hospital.

There had been no previous serious illness. The first pregnancy four years before admission had resulted in a miscarriage. Two years later a normal infant was born at full term.

On examination the patient was comatose, responding only to extremely painful stimuli. The pupils were markedly constricted. There was a purulent exudate in the nasal tract. The throat was red. Respirations were labored at 30 per minute. Breath sounds were diminished at the right lung base, and a few moist rales were heard low in both axillas. A soft apical systolic murmur and a Grade II systolic murmur were heard in the pulmonic area. The liver and spleen were not palpable. The uterine fundus rose to the level of the umbilicus. The fetal heart sounds were regular at a rate of 140 per minute. There was no vaginal discharge. The skin was clear, and no edema of the extremities was evident. The neck was not stiff, but the patient groaned when it was flexed. The tendon reflexes were hyperactive in the arms and in the left leg. There was no ankle clonus. The plantar reflex was equivocal on the right, and definitely extensor on the left.

The temperature was 99.8°F., the pulse 128, and the blood pressure 100 systolic, 60 diastolic.

Examination of the blood disclosed a hemoglobin of 12 gm. per 100 cc. and a white-cell count of 33,100, with 96 per cent neutrophils. The fasting blood sugar was 215 and the nonprotein nitrogen 22 mg. per 100 cc., the carbon dioxide 16, the chloride 102 and the sodium 131.8 milliequiv. per liter. The urine gave a +++ test for albumin. The sediment contained 3 to 5 white cells, rare red cells and 3 to 5 granular casts per high-power field. Thick, yellow spinal fluid was obtained by lumbar puncture. It contained 336,000 cells per cubic millimeter, with 95 per cent polymorphonuclears. Numerous gram-positive lancet-shaped diplococci demonstrated on a smear were identified as Type 4 pneumococci. The same organism was grown from the blood. The spinal-fluid sugar was 16 and the protein 940 mg. per 100 cc.; the chloride was 112 milliequiv. per liter. X-ray examination of the chest showed elevation of the right half of the diaphragm and mottled areas of increased density extending from low in the right hilus into the right costophrenic sinus. On the lateral view the right middle lobe appeared unusually dense.

Treatment consisted of intravenous and intrathecal penicillin and intravenous sulfadiazine and fluids. The spinal fluid gradually became less cloudy, and by the eleventh hospital day, it was clear and sterile, the sugar being 69 mg. per 100 cc. and the cell count 40 lymphocytes per cubic millimeter.

The patient's condition, however, did not correspond to the improved spinal-fluid findings. She never regained consciousness. Sulfadiazine had to be stopped twice because of oliguria and hematuria, although the urinary output never ceased completely. No rise in the nonprotein nitrogen resulted. Type 4 antipneumococcus rabbit serum injected on the third day apparently caused a rapid fall in the temperature to normal, but only a small amount of the serum was available. The temperature then ran between 99 and 101°F. until the eleventh day, when it was again normal. There was some fluctuation in the lung signs, the rate and character of respirations and the depth of the coma, but at no time were the lungs free from signs of consolidation or atelectasis. On one occasion the extensor plantar response shifted from the left to the right; otherwise, there was no significant change in the neurologic signs. A male infant was born on the tenth day and lived only six hours.

On the thirteenth day the temperature began to rise, reaching 104 to 105°F., where it remained. The respirations were labored and rapid. On spinal puncture 30 cc. of cloudy fluid containing 720 cells per cubic millimeter was obtained. No organisms grew from it. Terminally the count rose to 1200 cells per cubic millimeter, with 85 per cent polymorphonuclears. The patient died on the seventeenth day, having remained in coma during the entire period of hospitalization.

Differential Diagnosis

Dr. Wyman Richardson: I do not usually ask questions, but there are a few that I should like to have answered in this case. The first is whether the pupils remained constricted or whether that condition can be attributed to morphine. Was the blood sugar taken before or after intravenous glucose was given? It is quite important to know whether the blood sugar was really elevated or whether the elevation was due to intravenous glucose. Is there any record of sulfonamide therapy during this period? How long after morphine was this examination done? The record indicates a considerable lapse of time, but I am not sure of that.

There is a little too much stress on the oliguria in this abstract.

The Babinski sign or plantar reflex, to my mind, is always equivocal so far as the diagnosis is concerned.

The hemoglobin was a low normal for a nonpregnant person. The blood picture, I suppose, is consistent with infection.

"At no time were the lungs free from signs of consolidation." No signs of consolidation were recorded, so far as I can make out. There were diminished breath sounds and rales on one occasion, but consolidation is not mentioned.

"On one occasion the extensor plantar response shifted from the left to the right." Just like it!

A brief discussion of the symptoms is indicated. The onset of headache suggests the possibility of sinusitis. The history of the early oliguria, in spite of the adequate fluid intake, is something that must be explained. The clinical history is not suggestive of lobar pneumonia. There was a moderate acidosis, with a low carbon dioxide and a low blood sodium. I should like to ask Dr. Butler at this point about the chloride of 102 milliequiv. per liter. What happens to the chloride when the sodium is low? I should think that the chloride would have to be low.

Dr. Allan M. Butler: Sodium and chloride are almost entirely independent. In plasma there are a variety of positively charged ions and a variety of negatively charged ions that exist almost totally dissociated as ions and are not combined as molecules.

Dr. Richardson: But the total has to be balanced?

Dr. Butler: Yes; the total positive and negative ions must balance. In this patient the carbon dioxide was reduced from the normal of 26 to 16 milliequiv. per liter. The chloride was normal. The sodium was somewhat low, but it is hard to say how low, because there is a variation in the normal sodium concentration of 136 to 147 milliequiv. per liter by the method used in this case, just as there is a variation in the normal chloride from 100 to 107 milliequiv. per liter. The carbon dioxide may have been low because there was hyperventilation with the meningitis. Such hyperventilation would also tend to lower the sodium and to raise the chloride. Also, the ketosis of starvation might tend to lower the carbon dioxide. Thus, the changes in electrolyte concentrations are consistent.

The thing that is important is to use this case as a plea to stop asking the laboratory to test the spinal-fluid chloride when there is no possible information to be obtained from it. Unless one is dealing with a possible diagnosis of tuberculous meningitis, there is no rhyme or reason for requesting that determination, and even in cases of tuberculous meningitis, the chloride is of no help unless a simultaneous serum chloride is tested.

Dr. Richardson: I shall call attention to the lack of rise in the nonprotein nitrogen. And no dysuria was reported at any time.

With some diffidence, I am going to criticize the treatment. I do not like to do this as a rule, because hindsight is easier than foresight. I wonder, however, whether it was justifiable, in spite of the severity of the infection, to use the sulfonamides in the face of a marked oliguria. I should like to ask what the output was. And I should like to know whether or not the elevated blood sugar was important. I have in mind the possibility that the patient had moderate diabetes, which might have led to certain diseases. According to this chart that Dr. Mallory has shown me, the output during the middle of the course of the illness was fairly good.

Dr. Tracy B. Mallory: I think that the oliguria followed the sulfonamide treatment rather than preceded it.

Dr. Richardson: The output was over 1500 cc., and one might be justified in giving sulfonamide in such a desperately sick patient. Another criticism is that there was a distinct likelihood of intracranial pressure and of cerebral disease in this patient, but from the record the possibility does not seem to have been investigated. There was undoubtedly some good reason, however. I think that there were lesions in the spinal canal and brain, possibly in the kidneys and possibly in the lungs. In the spinal canal we know that there was an acute purulent meningitis, due to the Type 4 pneumococcus. Was there disease in the brain? Pneumococcal meningitis could have resulted in obstruction at the foramen of the fourth ventricle — what do you call it, Dr. Kubik?

Dr. Charles S. Kubik: The foramen of Magendie and Luschka.

Dr. Richardson: Obstruction can occur at that point and does so in certain types of meningitis, with a resulting internal hydrocephalus. Constricted pupils may, I believe, point to midbrain lesions. Dr. Kubik will check me on that. This is the only evidence I find of localization of a brain lesion. On the other hand there is a distinct suggestion of sinusitis

in this case, and it is quite probable that the coma, which was the presenting symptom and never cleared, was due to a brain lesion, with increased intracranial pressure. The question is, Just what type of obstruction due to meningitis was this? Was it caused by a lesion pressing at the base of the brain? There is a definite possibility that this patient had a localized lesion. I suspect that the trouble started with ethmoiditis or infection in the sinuses, including the ethmoid, and I think that there might have been a localized abscess in the brain. There is little evidence on which to base such a diagnosis, except that the patient did not get well.

What about the kidneys, which seem to have been involved? In pregnancy the lesion described as diffuse cortical necrosis may occur. Terminally, there does not seem to be enough renal failure to allow for such a diagnosis. Recently, Robbins, Mallory and Kinney* described a disease known as necrotizing papillitis. Their cases occurred in conjunction with a severe infection in diabetic patients, and were not necessarily associated with pregnancy. One might consider glomerulonephritis as a result of infection, but, again, the picture in the case under discussion does not seem to have been that of glomerulonephritis. I think that the kidneys will show multiple abscesses, as a result of a septicemia due to the pneumococcus. There is no evidence of pyuria to go with multiple infections in the kidneys, but this possibility must be considered. Finally, it must be determined whether this patient had a sulfonamide nephrosis, with some renal failure. All the conditions that I have mentioned are questionable. I do not know how to make a definite statement.

What about the lung? I do not believe that there was any disease in the lung.

DR. RICHARD SCHATZKI: There is one more film taken in bed in which there is definite abnormality in the right middle lobe, which is markedly decreased in size. There is atelectasis in the middle lobe and, in addition, disease in the lower lobe that also looks like atelectasis.

DR. RICHARDSON: I am going to forget about the lungs. I think that they were "wet." I do not see clinical or x-ray evidence of pneumonia. There could have been a lesion to account for metastases to the brain or for meningitis. I do not see it. I say that this patient had a meningitis due to a Type 4 pneumococcus. I am sure of that. I believe that the cerebral lesion was an abscess, probably arising from a sinusitis. The kidneys will show small abscesses and possibly a sulfonamide nephrosis.

DR. BUTLER: So far as the therapy is concerned, I should argue that it was correct to use the sulfonamides and penicillin. In administering sulfadiazine one ought, of course, to see to it that everything is done to maintain a proper urine volume. I do not believe that a urine volume of 1500 cc. must be present before one is justified in giving sulfonamides to such a patient as this. As I look at the chart of the urine output, the treatment appears justified.

DR. MALLORY: The sulfonamides were given in two periods. The urinary output dropped, and treatment was stopped; it went up, and the sulfonamides were tried again.

DR. RICHARDSON: I am sure that there is going to be something wrong with the kidneys.

CLINICAL DIAGNOSES

Meningitis due to Type 4 pneumococcus.
Bronchopneumonia.

DR. RICHARDSON'S DIAGNOSES

Acute ethmoiditis.
Acute meningitis (Type 4 pneumococcus).
Brain abscess.
Multiple renal abscesses.
Sulfonamide nephrosis?

ANATOMICAL DIAGNOSES

Acute sinusitis, left ethmoid and sphenoid.
Bacterial endocarditis, mitral valve (Type 4 pneumococcus).
Multiple infarcts and abscesses of brain.
Meningitis, pneumococcal, healing.
Infarct of heart.
Infarct of left kidney, healing.
Bronchopneumonia, slight.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The primary lesion at autopsy was not mentioned by Dr. Richardson, although he foretold many of the complications. It was an acute bacterial endocarditis of the mitral valve consequent to a pneumococcal septicemia that the patient had had at the start of the illness. Dr. Richardson was correct in suspecting underlying sinusitis. There was severe chronic infection of the left ethmoid and sphenoid sinuses. There was little in the lung other than considerable atelectasis and a few small patches of terminal pneumonia. The long coma was explained when we examined the brain — there was almost no anatomical evidence of persisting meningitis, but on section innumerable areas of softening throughout the white matter were found, many of which seemed primarily to be infarction but a few of which contained enough leukocytes to be classified as abscesses. There had also been an embolism of the coronary arteries, and a considerable area of infarction was found. The kidneys were perfectly normal except for one small, almost healed infarct.

DR. RICHARDSON: I do not see why you call bacterial endocarditis the primary lesion. I should think that it was secondary to the sinus infection, with septicemia, and then an implantation.

DR. MALLORY: Yes; the sinuses were the portal of entry of the infection, but the endocarditis and the consequent multiple septic emboli to the brain were the basic lesions accounting for death.

*Robbins, S. L., Mallory, G. K., and Kinney, T. D. Necrotizing renal papillitis: form of acute pyelonephritis. *New Eng. J. Med.* 235:885-893, 1946.

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THE RED CROSS: A HEALTH-PROMOTING AGENCY

The opening rally of the 1947 Greater Boston Red Cross Fund will be held on February 27 at Symphony Hall. From then through March 26 all residents and workers of Greater Boston are being asked to contribute to the $1,280,000 that is Greater Boston's part of the $60,000,000 to be raised nationally by this great humanitarian organization. Of all money contributed, 75 per cent will go to serve veterans, servicemen and their families. The remainder will go for those regular Red Cross services of disaster relief, water safety, first aid, nutrition, nursing, transportation and other health and educational activities.

The American Red Cross is carrying a heavy load of responsibilities accumulated during the war. It is helping to fulfill the many promises made by grateful citizens to their servicemen by aiding veterans both in hospitals and in their homes. The Army, Navy and Veterans Administration have provided for meeting the basic needs of the men and women in their installations. Situations arise, however, when there is need for equipment and supplies that cannot be obtained through official sources. As physicians are the first to realize, recovery from both physical and mental illnesses often depends on more than medicine or the best surgical skill. At the request of regular hospital personnel, the Red Cross provides carefully trained workers to help speed return to health and usefulness. It also furnishes supplies and equipment for making recovery and rehabilitation quicker and easier.

Despite continued nursing shortages nationally, 852 nurses served under Red Cross direction in seventy-four disasters in thirty-six states during 1945–1946. Sixteen floods in as many states, sixteen tornadoes in fifteen states, fourteen epidemics in thirteen states and thirteen major fires in nine states led the list of fiscal catastrophes. Disasters with proportionately fewer nursing needs were train wrecks, explosions, hurricanes and bus and other accidents.

The Red Cross also carried on a home-nursing program to promote better family and community health. Such training includes instruction in personal health, the care of mother and baby and the control of communicable diseases in the home and community. The objective is to train one person in every home to take care of minor illnesses under the doctor's orders and to realize that a minor illness may become a major illness unless proper nursing and medical care are given.

Red Cross public-health nursing services have been established in rural areas and small towns where other local health agencies had no plans or possibilities for organizing such a service. These public-health nursing services are established only after a careful study of community needs, consultation with state and local departments of health and the approval of the Area Red Cross office.

Red Cross first-aid training develops the knowledge and skill necessary for the care of the victim of an accident or sudden illness until the services of

a physician can be obtained. It has often meant the difference between life and death, between temporary and permanent disability or between rapid recovery and long hospitalization. It is also an important part of industrial safety programs, and reports from throughout the Nation indicate that such training frequently curtails the number of lost-time accidents by as much as 50 per cent.

The Red Cross is a health-promoting agency — in the home, in the hospital, on the highway. It gives food to those in other countries left starving by war and disaster. It teaches food preservation and good nutrition to the housewives of this country. Its financial assistance helps many a veteran's or serviceman's family when the need arises or over a temporary period until a Government claim or other plan can be established. It also brings comfort, nursing service and help to veterans, servicemen and civilians in hospitals throughout the country. In other words, the Red Cross gives service and help wherever there is need. Physicians should continue to support this great humanitarian organization!

Q FEVER

During the past two years, while the search continued for the agent or agents that are responsible for the disease known as "virus pneumonia," considerable information has accumulated concerning the occurrence of the specific rickettsial disease Q fever as a cause of some severe types of atypical pneumonia. Most of the new information regarding this disease was collected by workers in Army hospitals and laboratories and has been published only recently. The identity of the agent and some aspects of its epidemiology and pathogenicity have come to light during the last decade.

In 1937, Derrick[1] described an influenza-like infection occurring among meat workers that had come into prominence since 1935 in Queensland, Australia; he called the disease "Q fever." The causative agent was isolated by the intraperitoneal injection of guinea pigs with the blood and urine obtained from patients during the acute stage of the disease. The agent was studied in detail by Burnet and Freeman,[2] who showed it to be a filter-passing rickettsia. They showed that specific antibodies developed toward the end of the second week of illness and could be demonstrated by the agglutination of suitable suspensions of the rickettsia. Infection with the rickettsia was found to be widespread in a native rodent, the bandicoot, which served as a reservoir, with certain ticks acting as vectors. Forest workers and cattle were infected directly by infected ticks, and slaughterhouse workers were thought to be infected by the inhalation of dried feces of ticks infected from the cattle.[3] Pneumonia was not recognized as a feature of Q fever in the Australian cases. The organism was named *Rickettsia burneti*.

An agent similar to *R. burneti* was isolated at about the same time by workers in the Rocky Mountain Laboratory of the United States Public Health Service from ticks collected in Montana and Wyoming.[4] A disease corresponding to Australian Q fever is known to occur in this area, and serologic evidence of infection with the agent was found in persons over a large area of the United States, ranging from Nebraska to Texas and Washington.[5] In 1940, an outbreak of pneumonitis due to the organism of Q fever occurred at the National Institute of Health in Bethesda, Maryland.[6]

The studies made by the Army workers have been recently reported in detail.[7] During the winter of 1944–1945 outbreaks of severe atypical pneumonia occurred among British troops stationed in the Mediterranean area and also among American military units in Corsica. The disease differed in some important respects from the atypical pneumonia that was prevalent in the United States and Great Britain. It seemed to be sharply limited to particular units and areas and was characterized by a high attack rate, — up to 50 per cent, — and there was no associated increase in cases of minor respiratory illnesses. The clinical and epidemiologic findings were readily corroborated when an opportunity arose to investigate an outbreak among the members of a British parachute regiment who had acquired the infection in Athens. Although the studies in that outfit began when the outbreak was subsiding, it was possible to identify its nature in retrospect by the laboratory examination of serum specimens from patients.

Four similar outbreaks were investigated among American military units stationed in Italy near Florence and Bologna. The rickettsia of Q fever was isolated from the blood of some of the patients in these outbreaks and was shown to be the cause of the outbreaks. At the same time it was demonstrated serologically that about three fourths of the sporadic cases of atypical pneumonia in the same region were, in fact, cases of Q fever. These laboratory studies were carried out chiefly in the Fifteenth Medical General Laboratory, which was serving this area.

At about the same time it was also learned that an outbreak of a severe influenza-like infection associated with atypical pneumonia had occurred during the preceding winter in Athens. The Germans, who seemed to be more severely affected than the natives, called it the "Balkan grippe." Dr. J. Caminopetros, of the Pasteur Institute of Greece, was able to establish a transmissible febrile illness in guinea pigs by the inoculation of blood from a patient obtained during the acute stage of the disease. One of these guinea pigs was later brought to the laboratories of the Commission on Acute Respiratory Disease at Fort Bragg, North Carolina, where the rickettsia of Q fever was isolated and identified.

During May and June, 1945, other outbreaks occurred among certain units that were being returned to the United States from southern Italy. One of these was studied by the medical officers at Camp Patrick Henry, Virginia, and the etiologic and epidemiologic aspects were investigated by the Commission on Acute Respiratory Diseases. The cause of this outbreak was identified as the Balkan-grippe type of *R. burneti*.

Outbreaks of severe atypical pneumonia occurred among the personnel of the two laboratories in which these investigations were being carried out. The one in the Fifteenth Medical General Laboratory was shown, by isolation of the agent and by serologic studies, to have been due to the Italian strain of *R. burneti*, and similar studies in the Fort Bragg laboratory indicated that the infections there were caused by the Balkan strain. There were no deaths among these cases.

Another possible focus of Q fever was suggested by the report of a case of atypical pneumonia in a military hospital in Panama. Serologic studies of the blood of the patient and of the agent that was isolated from the blood indicated that the disease was caused by a strain of the American type of Q fever. The patient had been in Panama for several months prior to his illness.

A preliminary report has also appeared about an outbreak of Q fever that occurred in Amarillo, Texas, in May, 1946.[8] There were more than 40 cases. Most of them occurred in men who were employees of a stockyard and meat-packing company, but some were observed among railroad workers and others around the stockyards. There were 2 deaths in this outbreak.

The strains of *R. burneti* isolated from the various outbreaks have many characteristics in common. Antigenic differences among these strains have been partially worked out by investigators at the National Institute of Health. These differences suggest that Q fever may be more prevalent in the United States than was previously suspected and that cases may have been missed because of the improper selection of strains for the serologic tests.

References

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2. Burnet, F. M., and Freeman, M. Experimental studies on virus of "Q" fever. *M. J. Australia* **2**:299-305, 1937.
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4. Davis, G. E., and Cox, H. R. Filter-passing infectious agent isolated from ticks. I. Isolation from *Dermacentor andersoni*, reactions in animals and filtration experiments. *Pub. Health Rep.* **53**:2259-2267, 1938.
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7. Robbins, F. C., and others. Q fever: series of twelve papers. *Am. J. Hyg.* **44**:1-182, 1946.
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MASSACHUSETTS MEDICAL SOCIETY

TREASURER'S OFFICE

All members should be reminded that the proportion of the refund returned to each district society is based on the number of dues paid by March 1 in that district, and also that the names of members who have not paid their dues by March 1 are automatically removed from the mailing list of the *Journal* until such dues are paid.

ELIOT HUBBARD, JR., *Treasurer*

DEATH

JOHNSON — Herbert L. Johnson, M.D., of Hadley, died January 22. He was in his eighty-eighth year.

Dr. Johnson received his degree from Bowdoin Medical School in 1884.

POSTGRADUATE LECTURE COURSE

The review Postgraduate Lecture Course, which has been arranged by the Committee on Postgraduate Medical Education, Massachusetts Medical Society, in co-operation with the Massachusetts Department of Public Health, will begin on March 3. The meetings will be held at Sanders Theater in Memorial Hall, Harvard University, Cambridge. These lectures are primarily designed for general practitioners, but medical officers, hospital interns and residents, and postgraduate and undergraduate medical students are cordially invited to attend. Recent progress in medicine will be discussed, and the speakers have been urged to present their subjects in a simple and direct manner and to emphasize diagnosis and treatment from the point of view of the physician in general practice.

All those who plan to attend but have not enrolled should do so immediately by either returning the post card recently forwarded to all physicians in Massachusetts or addressing a post card or letter directly to the Postgraduate Lecture Course Committee, Massachusetts Medical Society, 8 Fenway, Boston 15.

The detailed program for the course is as follows:

Review Lecture Course

Monday, March 3. *5:30–5:45.* Opening Remarks. Dwight O'Hara: president, Massachusetts Medical Society; dean, Tufts College Medical School.

Medical Aspects of Atomic Warfare. *Chairmen*: Shields Warren and Stafford L. Warren.

5:45–6:45. **Medical Implications of the Bikini Experiments.** Capt. George M. Lyon (MC), U.S.N.R., assistant to the Surgeon General, Navy Department: Washington, D. C.; representative, Bureau of Medicine and Surgery, U.S.N., Joint Task Force One.

7:00–7:30. **Buffet Supper.**

7:30–8:00. **The Pathology of Atomic-Bomb Injuries.** Shields Warren: formerly, director of medical research, Bikini Project; pathologist, New England Deaconess and New England Baptist hospitals.

8:00–8:30. **General Aspects of Atomic Energy.** Stafford L. Warren: formerly, medical director, Manhattan Project; professor of radiology, University of Rochester Medical School, Rochester, New York.

8:30–9:00. **Motion pictures of Bikini Experiment.**

Wednesday, March 5. Infectious Diseases. *Chairmen*: Maxwell Finland and Conrad Wesselhoeft.

3:00–3:35. **Rubella and Congenital Deformities — The present problem.** Conrad Wesselhoeft: physician-in-chief, Haynes Memorial, Massachusetts Memorial Hospitals; clinical professor of communicable diseases, Harvard Medical School and Boston University School of Medicine.

3:35–4:10. **Pneumonias.** Maxwell Finland: chief, Fourth Medical Service, and associate physician, Thorndike Memorial, Boston City Hospital; assistant professor of medicine, Harvard Medical School.

4:10–4:45. **Meningitis.** Louis Weinstein: visiting physician, Haynes Memorial, Massachusetts Memorial Hospitals; assistant professor of medicine, Boston University School of Medicine.

4:45–4:50. **Intermission.**

4:50–5:25. **Use of Gamma Globulin.** Charles A. Janeway: professor of pediatrics, Harvard Medical School; chief, Medical Service, Children's Hospital.

5:25–6:00. **Prophylactic Inoculations.** Geoffrey Edsall: instructor in bacteriology and applied anatomy, Harvard Medical School; assistant director, Division of Biologic Laboratories, Massachusetts Department of Public Health.

Monday, March 10. Part I. Chest Disease. *Chairmen*: Theodore L. Badger and Reeve H. Betts.

5:30–6:00. **The Role of Surgical Exploration in the Diagnosis and Treatment of Intrathoracic Lesions.** Reeve H. Betts: assistant professor of surgery, Tufts College Medical School.

6:00–6:30. **The Value of Streptomycin and BCG in the Treatment and Prevention of Tuberculosis.** Lowrey F. Davenport: instructor in medicine, Harvard Medical School.

6:30–7:00. **The Management of Suppurative Diseases of the Lung.** John W. Strieder: associate professor of surgery, Boston University School of Medicine; chief, Thoracic Surgery, Boston City Hospital; visiting surgeon in charge of thoracic surgery, Massachusetts Memorial Hospitals.

7:00–7:30. **Buffet Supper.**

Part II. Neurosurgical Disease. *Chairmen*: Gilbert Horrax and James C. White.

7:30–8:00. **The Neurosurgical Treatment of Pain.** James C. White: assistant professor of surgery, Harvard Medical School; chief of neurosurgical service, Massachusetts General Hospital.

8:00–8:30. **The Treatment of Spinal-Cord Injury.** Donald Munro: associate professor of neurosurgery, Boston University School of Medicine; assistant professor of neurosurgery, Harvard Medical School; surgeon-in-chief and Head of Department of Neurosurgery, Boston City Hospital.

8:30–9:00. **The Diagnosis and Treatment of Brain Tumors.** Gilbert Horrax: chief of Department of Neurosurgery, Lahey Clinic; neurosurgeon to New England Deaconess and New England Baptist hospitals.

Wednesday, March 12. Infantile Paralysis and Back Pain. *Chairmen*: William T. Green and Arthur A. Thibodeau.

3:00–3:25. **Epidemiology of Infantile Paralysis.** Charles A. Janeway: professor of pediatrics, Harvard Medical School; chief, Medical Service, Children's Hospital.

3:25–3:50. **Diagnosis and Early Care of Infantile Paralysis.** Thomas Gucker: assistant in orthopedic surgery, Children's Hospital.

3:50–4:15. **The Treatment of Infantile Paralysis during Convalescence.** David S. Grice: junior attending orthopedic surgeon, Children's Hospital and Peter Bent Brigham Hospital; assistant in Department of Orthopedics, Harvard Medical School; assistant director, Massachusetts Infantile Paralysis Clinics.

4:15–4:30. **The Chronic Stage of Infantile Paralysis — Rehabilitation.** William T. Green: assistant professor of orthopedics, Harvard Medical School; orthopedic surgeon-in-chief, Children's Hospital.

4:30–4:40. **Intermission.**

4:40–5:05. **Body Mechanics, Examination of the Back, Postural Back Ache.** James W. Toumey: orthopedic surgeon, Lahey Clinic, New England Baptist and New England Deaconess hospitals.

5:05–5:30. **Acute Back Strain and Other Causes of Back Pain.** Arthur A. Thibodeau: instructor in orthopedics, Tufts College Medical School.

5:30–6:00. **Sciatica and Rupture of Intervertebral Disk.** Joseph S. Barr: clinical professor of orthopedic surgery, Harvard Medical School; chief of Orthopedic Staff, Massachusetts General Hospital.

Monday, March 17. MINOR SURGERY AND SURGICAL SHOCK. *Chairmen*: Augustus Thorndike and C. Stuart Welch.

5:30–6:15. **Injuries of the Hand: Examination, diagnosis and early treatment.** Henry C. Marble: assistant in surgery, Harvard Medical School; visiting surgeon, Massachusetts General Hospital; surgeon-in-chief, Chelsea Memorial Hospital.

6:15–7:00. **Infections of the Skin — Pustular Acne, Furunculosis and Carbuncles.** Joseph Tartakoff: assistant professor of surgery, Tufts College Medical School; assistant visiting surgeon, Boston City Hospital.

7:00–7:30. **Buffet Supper.**

7:30–8:00. **Sprains, Strains and Contusions: Pathology and treatment.** Thomas B. Quigley: associate in surgery, Harvard Medical School and Peter Bent Brigham Hospital.

8:00–8:30. **Surgical Shock.** John E. Dunphy: associate in surgery, Harvard Medical School; visiting surgeon, Peter Bent Brigham Hospital.

8:30–9:00. **Burns of the Hand: Early and late treatment.** Melvin F. White: assistant professor of surgery, Tufts College Medical School; visiting surgeon, St. Elizabeth's Hospital; plastic surgeon, Tumor and Surgical Departments, Boston Dispensary.

Wednesday, March 19. ANESTHESIA AND ITS COMPLICATIONS. *Chairmen*: Henry K. Beecher and Morris J. Nicholson.

3:00–3:40. **Current Trends in the Use of General Anesthesia.** M. Gene Black: anesthetist, Massachusetts Memorial Hospitals; instructor in anesthesiology, Boston University School of Medicine.

3:40–4:20. **Management of the Patient under Spinal Anesthesia.** Leo V. Hand: anesthetist, New England Deaconess Hospital.

4:20–4:40. **Intermission.**

4:40–5:20. **Postanesthetic Complications.** Morris J. Nicholson: Department of Anesthesiology, Lahey Clinic; anesthetist, New England Deaconess and New England Baptist hospitals.

5:20–6:00. **Evaluation and Care of the Patient in Shock.** Henry K. Beecher: anesthetist-in-chief, Massachusetts General Hospital; Henry I. Dorr Professor of Research in Anesthesia, Harvard Medical School.

Monday, March 24. ENDOCRINOLOGY, INCLUDING DIABETES. *Chairmen*: Richard P. Stetson and George W. Thorn.

5:30–6:00. **Carbohydrate Metabolism: Recent concepts.** Richard P. Stetson: associate in medicine, Harvard Medical School; assistant visiting physician, Boston City Hospital.

6:00–6:30. **Diabetes Mellitus: Degenerative complications.** Alexander Marble: instructor in medicine, Harvard Medical School; physician, New England Deaconess Hospital.

6:30–7:00. **Adrenal Insufficiency: Diagnostic criteria.** George W. Thorn: Hersey Professor of Theory and Practice of Physic, Harvard Medical School; physician-in-chief, Peter Bent Brigham Hospital.

7:00–7:30. **Buffet Supper.**

7:30–8:00. **Thyrotoxicosis — Pathologic Physiology.** Rulon W. Rawson: associate in medicine, Harvard Medical School; assistant physician, Massachusetts General Hospital.

8:00–8:30. **Thyrotoxicosis — Evaluation of Treatment with Thiouracil Compounds.** Robert H. Williams: associate in medicine, Harvard Medical School; junior visiting physician, Boston City Hospital.

8:30–9:00. **Postmenopausal Osteoporosis.** Fuller Albright: associate professor of medicine, Harvard Medical School; physician, Massachusetts General Hospital.

Wednesday, March 26. GYNECOLOGY AND STERILITY. *Chairmen*: Samuel R. Meaker and Fred A. Simmons.

3:00–3:25. **Management of Dysmenorrhea.** Somers H. Sturgis: assistant surgeon, Massachusetts General Hospital; assistant in gynecology, Harvard Medical School.

3:25–3:50. **Habitual Abortion.** Arthur T. Hertig: pathologist, Boston Lying-in Hospital and Free Hospital for Women; assistant professor of pathology and obstetrics, Harvard Medical School.

3:50–4:15. **Ovulation Timing.** Fred A. Simmons: assistant surgeon, Massachusetts General Hospital and Free Hospital for Women; assistant in gynecology, Harvard Medical School.

4:15–4:30. **Intermission.**

4:30–5:00. **Depressed Respiratory Metabolism and Low Fertility.** Samuel R. Meaker: gynecologist, Massachusetts Memorial Hospitals; professor of gynecology, Boston University School of Medicine.

5:00–5:30. **Ovarian Hormone Therapy.** Max Davis: obstetrician and gynecologist, Massachusetts Memorial Hospitals; assistant professor of obstetrics and gynecology, Boston University School of Medicine.

5:30–6:00. **Findings and Results in a Series of Sterility Cases.** A. Seymour Parker, Jr.: physician, Medical Department, Lahey Clinic.

Monday, March 31. OBSTETRICS. *Chairmen*: Roy J. Heffernan and Frederick C. Irving.

5:30–5:50. **Diet in Pregnancy.** Bertha L. Burke: assistant professor of maternal and child nutrition, Harvard School of Public Health.

5:50–6:20. **The Rh Factor.** Louis K. Diamond: assistant professor of pediatrics, Harvard Medical School; visiting physician, Children's Hospital.

6:20–6:40. **New Developments in Prenatal Care.** Charles L. Sullivan: assistant obstetrician, St. Elizabeth's Hospital and Massachusetts General Hospital.

6:40–7:00. **Induction of Labor.** Roy J. Heffernan: visiting obstetrician and gynecologist, Carney Hospital; consulting obstetrician and gynecologist, Faulkner Hospital and St. Margaret's Hospital.

7:00–7:30. **Buffet Supper.**

7:30–7:50. **The Use of X-Ray in Obstetrics.** Daniel J. McSweeney: assistant professor of obstetrics, Boston University School of Medicine and Tufts College Medical School; visiting obstetrician, Boston City Hospital and St. Margaret's Hospital.

7:50–8:10. **The Fetus during Labor.** Charles L. Sullivan.

8:10–8:30. **Extrauterine Pregnancy.** Daniel J. McSweeney.

8:30–8:50. **Indications for Forceps Delivery.** Roy J. Heffernan.

Wednesday, April 2. GASTROENTEROLOGY. *Chairmen*: Franz J. Ingelfinger and Chester M. Jones.

3:00–3:25. **Procedures in Diagnosis and Management of Peptic Ulcer.** Franz J. Ingelfinger: associate professor of medicine, Boston University School of Medicine; chief, Gastrointestinal Outpatient Department, Massachusetts Memorial Hospitals; member of staff, Robert Dawson Evans Memorial Hospital.

3:25–3:50. **Medical Management of Peptic Ulcer.** Sara M. Jordan: director of gastroenterology, Lahey Clinic; physician, New England Baptist and New England Deaconess hospitals.

3:50–4:15. **Surgical Management of Peptic Ulcer.** Francis D. Moore: associate in surgery, Harvard Medical School; assistant surgeon, Massachusetts General Hospital.

4:15–4:30. **Intermission.**

4:30–5:05. **Diagnostic and Medical Measures Pertinent to the Problem of Painless Jaundice.** Chester M. Jones: clinical professor of medicine, Harvard Medical School; physician, Massachusetts General Hospital.

5:05–5:40. **Surgical Measures in Relation to Painless Jaundice.** Reginald H. Smithwick: professor of surgery, Boston University School of Medicine; surgeon-in-chief, Massachusetts Memorial Hospitals; member of board of consultants, Massachusetts General Hospital.

5:40–6:00. **Discussion.**

Monday, April 7. PART I. OFFICE PROCEDURES IN ANORECTAL DISEASE. *Chairmen*: E. Parker Hayden and Neil W. Swinton.

5:30–5:45. **Differential Diagnosis of Rectal Bleeding and Methods of Rectal and Colon Examinations.** E. Parker Hayden: chief, Proctologic Clinic, and assistant visiting surgeon, Massachusetts General Hospital.

5:45–6:00. **Hemorrhoids.** Roy E. Mabrey: assistant surgeon, Massachusetts General Hospital.

6:00–6:10. **Anal Fissure.** Roy E. Mabrey.

6:10–6:25. **Anorectal Abscess and Fistula.** E. Parker Hayden.

6:25–6:40. **Premalignant Lesions of the Rectum and Colon.** Neil W. Swinton: surgeon, Lahey Clinic, New England Deaconess and New England Baptist hospitals.

6:40–7:00. **Anal Pruritus.** Neil W. Swinton.

7:00–7:30. **Buffet Supper.**

PART II. RADIATION THERAPY. *Chairmen*: Joseph H. Marks and Samuel A. Robins.

7:30–7:45. **Contact Therapy of Superficial Lesions.** Bernard E. LeVine: radiation therapeutist, Beth Israel Hospital.

7:45–8:00. **Hodgkin's Disease.** Hugh F. Hare: director, Department of Radiology, Lahey Clinic.

8:00–8:15. **Fibroids and Menorrhagia.** Samuel A. Robins: professor of radiology, Tufts College Medical School; chief radiologist, Beth Israel Hospital and Evangeline Booth Hospital.

8:15–8:30. **Carcinoma of the Cervix.** Laurence L. Robbins: roentgenologist, Massachusetts General Hospital.

8:30–8:45. **Carcinoma of the Ovary.** Joseph H. Marks: instructor in radiology, Harvard Medical School; radiologist, New England Deaconess and Palmer Memorial hospitals.

8:45–9:00. **Discussion.**

Wednesday, April 9. DISEASES OF BLOOD AND LYMPH NODES. *Chairmen*: William Dameshek and Thomas H. Ham.

3:00–3:30. **Diagnosis of Anemia.** Thomas H. Ham: assistant professor of medicine, Harvard Medical School; associate physician, Thorndike Memorial, and junior visiting physician, Boston City Hospital.

3:30–4:00. **Treatment of the Anemias.** Maurice B. Strauss: chief of medical service, Cushing General Hospital, Framingham.

4:00–4:35. **Diagnosis and Treatment of Disorders of the Spleen.** William Dameshek: professor of clinical medicine, Tufts College Medical School; hematologist, Pratt Diagnostic Hospital; chief, Blood Clinic, Boston Dispensary.

4:35–4:45. **Intermission.**

4:45–5:15. **Treatment of Leukemia.** Henry Jackson, Jr.: associate physician, Thorndike Memorial, Boston City Hospital; assistant professor of medicine, Harvard Medical School.

5:15–5:45. **Transfusion Therapy.** Charles P. Emerson: assistant professor of medicine, Boston University School of Medicine; member of staff, Massachusetts and Evans Memorial hospitals.

5:45–6:00. Discussion.

Monday, April 14. THE PREVENTION OF VENOUS THROMBOSIS AND PULMONARY EMBOLUS. *Chairmen*: Arthur W. Allen, James A. Evans and John Homans.

5:30–6:00. **Clinical Features of Pulmonary Embolism.** Lewis Dexter: assistant in medicine, Harvard Medical School; senior associate in medicine, Peter Bent Brigham Hospital.

6:00–6:30. **Experiences with Heparin in Pitkin's Menstruum Combined with Dicumarol in the Treatment of Venous Thrombosis.** James A. Evans: physician, Lahey Clinic; physician, New England Baptist and New England Deaconess hospitals.

6:30–7:00. **Anticoagulant Drugs versus Vein Ligation in the Treatment of Thrombophlebitis at the Beth Israel Hospital.** Arnold Starr: junior visiting surgeon, Beth Israel Hospital.

7:00–7:30. **Buffet Supper.**

7:30–8:00. **Three-year Study of Rest, Exercise and Early Ambulation Relative to Venous Thrombosis: Analysis of 2000 consecutive cases.** James C. McCann: surgeon, St. Vincent's Hospital, Worcester.

8:00–8:30. **Prophylactic Femoral-Vein Division at the Massachusetts General Hospital.** Robert R. Linton: visiting surgeon and chief, Peripheral Vascular Clinic, Massachusetts General Hospital; associate in surgery, Harvard Medical School.

8:30–9:00. **The Prophylactic Use of Dicumarol in Gynecology.** George Van S. Smith: professor of gynecology, Harvard Medical School; chief, Free Hospital for Women.

Wednesday, April 16. PART I. KIDNEY DISEASE. *Chairmen*: Reginald Fitz and W. Richard Ohler.

3:00–3:30. **Diagnosis of Renal Disease.** Laurence B. Ellis: associate in medicine, Harvard Medical School; assistant visiting physician, Boston City Hospital.

3:30–4:30. **Treatment of Renal Disease.** Reginald Fitz: lecturer on the history of medicine, Harvard Medical School; consulting physician, Peter Bent Brigham Hospital; and W. Richard Ohler, assistant professor of medicine, Harvard Medical School; chief, Second Medical Service, Boston City Hospital.

4:30–4:35. **Intermission.**

PART II. HYPERTENSION. *Chairmen*: Robert S. Palmer and Reginald H. Smithwick.

4:35–5:00. **The Heart in Hypertension.** Paul D. White: clinical professor of medicine, Harvard Medical School; physician, Massachusetts General Hospital.

5:00–5:30. **The Value of Various Therapeutic Measures in the Management of Hypertension and Hypertensive Cardiovascular Disease.** Robert S. Palmer: associate physician, Massachusetts General Hospital; consultant, Massachusetts Eye and Ear Infirmary.

5:30–6:00. **Surgical Measures in Hypertensive Patients.** Reginald H. Smithwick: professor of surgery, Boston University School of Medicine; surgeon-in-chief, Massachusetts Memorial Hospitals.

Monday, April 21. CARDIOVASCULAR DISEASES. *Chairmen*: Samuel A. Levine and Howard B. Sprague.

5:30–6:00. **Pericarditis.** Howard B. Sprague: instructor in medicine, Harvard Medical School; associate physician, Massachusetts General Hospital; chief of medicine, House of the Good Samaritan.

6:00–6:30. **The Diagnosis of Coronary-Artery Disease.** James M. Faulkner: professor of medicine, Tufts College Medical School.

6:30–7:00. **The Treatment of Cardiac Emergencies.** Paul D. White: clinical professor of medicine, Harvard Medical School; physician, Massachusetts General Hospital.

7:00–7:30. **Buffet Supper.**

7:30–8:00. **The Clinical Features of Patent Ductus Arteriosus.** Samuel A. Levine: assistant professor of medicine, Harvard Medical School; physician, Peter Bent Brigham Hospital.

8:00–8:30. **The Heart in Acute Infections.** Charles A. Janeway: professor of pediatrics, Harvard Medical School.

8:30–9:00. **The Treatment of Subacute Bacterial Endocarditis.** Chester S. Keefer: professor of medicine, Boston University School of Medicine; director, Evans Memorial, Massachusetts Memorial Hospitals.

Wednesday, April 23. PEDIATRICS. *Chairmen*: Stewart H. Clifford and Richard C. Tefft, Jr.

3:00–3:45. **Influenza Meningitis: Diagnosis and treatment.** John A. V. Davies: assistant professor of pediatrics, Harvard Medical School.

3:45–4:30. **Factors Influencing the Growth and Development of the Fetus.** Clement A. Smith: assistant professor of pediatrics, Harvard Medical School.

4:30–4:40. **Intermission.**

4:40–5:15. **Influence of Disease on the Growth and Development of the Child.** Stuart S. Stevenson: associate in child health, Harvard Medical School and Harvard School of Public Health.

5:15–6:00. **Influence of Endocrine Dysfunction on Acceleration or Retardation of Growth and Development in the Child and Adolescent.** Nathan B. Talbot: assistant professor of pediatrics, Harvard Medical School.

CORRESPONDENCE

PSYCHOSOMATIC MEDICINE

To the Editor: I really enjoyed the excellent editorial on the meaning of psychosomatic medicine, which appeared in the January 9 issue of the *Journal*. In numerous places I have protested against the absurdities that the term "psychosomatic medicine" has somehow launched into clinical thinking. The effect of emotions, as organic events, on bodily structure is as old as Hippocrates, and long before Dunbar's book this was stressed in the literature by both experimental and clinical workers. Of course, all emotions are potent organic events, just as all experience changes bodily structure either transiently or permanently.

It is a far cry from this, however, to the fantastic ideas that the psychosomaticists have introduced into medicine. A misstep morally makes one slip on the ice twenty years later and break an ankle or the neck as a punishment self-inflicted by unconscious guilt. All kinds of nonstatistical and utterly unproved work asserts that this or that aggressive or nonaggressive trait is responsible for accidents, heart disease, ad lib, ad glib, and ad nauseum. The pediatricians, the orthopedic surgeons, the internists, indeed all kinds of physicians have taken it up so that, as one lady expressed it to me recently, it is rather dangerous to consult about a bodily disease at present, for you are accused of all kinds of things that have occurred in your childhood.

I plead guilty, for I have already introduced the word "somatopsychics" into the literature via two papers, one of which was published with that name as part of the title. I agree that neither psychosomatics nor somatopsychics is a necessary word. I believe, however, that merely stating that an experience, of whatever sort, creates bodily disorder is insufficient since the "experiencer" is as important as the "experience." There are people with constitutions predisposed to fear, depression and disastrous somatic responses to experience. Whether the constitution is acquired early through conditioning or inheritance is important, but the treatment does not depend finally and fundamentally on psychologic grounds — it rests on reorganizing physiology. That there is a bodily basis to the mental diseases, whether they are organic or functional is, so far as I am concerned, the proper working hypothesis of psychiatry. Every emotional experience activates bodily changes, and even if mental disease can be traced to emotional experiences, the bodily changes would still have to be understood and accounted for to bring about cure.

Psychosomatics talks much but cures little. The real therapeutic triumphs in psychiatry, as yet imperfect, are physiologic — insulin coma, electric and metrazol shock, prefrontal lobotomy and the use of Dilantin and other drugs. There are few who can live with an emotionally placid mood in an extremely troubled world.

ABRAHAM MYERSON, M.D.

171 Bay State Road
Boston 15

DEPRIVATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held January 16, it was voted to suspend the license to practice medicine of Dr. Marguerite Krausz, 8 Winter Street, Boston, for three months because of gross misconduct in the practice of her profession.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

BOOK REVIEWS

Local Health Units for the Nation: A report. By Haven Emerson, M.D. With the collaboration of Martha Lubinbuhl, M.A. 4°, paper, 333 pp., illustrated. New York: The Commonwealth Fund, 1945. $1.25.

This book is the report of the Subcommittee on Local Health Units of the Committee on Administrative Practice of the American Public Health Association. It discusses the existing local public-health services in the various states and makes suggestions for improved service. The book is largely composed of tables showing existing personnel and annual budgets for local health services, together with similar tables for an improved service. Each state is discussed separately.

This volume should be of value to health administrators, physicians and lay persons interested in improving public health.

Public Medical Care: Principles and problems. By Franz Goldman, M.D. 8°, cloth, 226 pp. New York: Columbia University Press, 1945. $2.75.

In this volume the author considers the problem of adequate medical care, describing the facilities that have been utilized in various countries in the past four centuries. The evolution of the public hospital, the transition from the primitive dispensary to the public medical center and the various methods employed in medical programs for persons in need are discussed.

In the last chapter the author outlines his solution of the problem as follows:

> It appears, then, that there is only one single method that would avoid the disadvantages inherent in other approaches to the problem of organizing payment for facilities and services: public medical care for all, with every necessary service provided as a right and free of charge. Such a system exists in Russia.

Regardless of whether one agrees or disagrees with the author's plan for medical care, his presentation of the changing patterns of medical service makes this book worth reading, and the extensive bibliography enhances its value.

Mitchell-Nelson Textbook of Pediatrics. Edited by Waldo E. Nelson, M.D. 4°, cloth, 1350 pp., with 519 illustrations, 26 in color. Fourth edition, revised. Philadelphia and London: W. B. Saunders Company, 1945. $10.00.

This composite authoritative standard treatise, the work of forty-nine contributors, first published in 1933 and last revised in 1941, has been completely rewritten and to all intents and purposes is a new book. Some alteration has been made in the general arrangement, a number of new sections have been added, and some sections of the previous editions have been discarded. It has been the aim of the editor to provide a textbook for the undergraduate medical student, the pediatrician and the general practitioner. The text is printed in a two-column format, with a good type on heavy paper. The volume because of its weight is difficult to handle. It is suggested that future editions or printings be made with a lighter paper, especially because the illustrations do not require the heavy paper. The book is recommended for all medical reference collections and to physicians interested in pediatrics.

The Physician's Business: Practical and economic aspects of medicine. By George D. Wolf, M.D. With a foreword by Harold Rypins, M.D. Second edition. 8°, cloth, 433 pp., with 58 illustrations. Philadelphia: J. B. Lippincott Company, 1945. $6.00.

Medicine is undoubtedly an altruistic profession in many ways, but the physician is entitled to a just compensation for his services. Dr. Wolf has analyzed medicine as a business and in this book has made his studies available to the medical profession. This second edition has been thoroughly revised wherever possible. New chapters on workmen's compensation laws and prepaid health insurance have been added, but the material on postgraduate study and war careers for physicians other than private practice have remained unaltered, because of the changing situation in these fields. The location of a practice, contacts with other physicians, specialization and the proper conduct of an office, including finance and insurance, are adequately discussed in a simple manner. There is an important chapter on the legal relations of the physician to his patients and the community. This book should prove of value to all physicians and should be in all medical and business libraries.

Hypnoanalysis. By Lewis R. Wolberg, M.D. With a foreword by A. Kardiner, M.D. 8°, cloth, 342 pp. New York: Grune and Stratton, 1945. $4.00.

The first part of this book comprises a complete report of a hypnoanalysis in an individual case of schizophrenia, with a dynamic interpretation of the protocol, involving the use of hypnosis as a therapeutic agent and resulting in a return of the patient to normal. The second is devoted to an extended consideration of the theory and practice of hypnoanalysis, including the relation of psychoanalysis and hypnosis.

The Psychoanalytic Theory of Neurosis. By Otto Fenichel, M.D. 8°, cloth, 703 pp. New York: W. W. Norton & Company, Inc., 1945. $7.50.

This book is in all respects an informative, systematized, reference text in psychoanalysis. The title is thus quite incomplete and perhaps misleading; not only the psychoanalytic theory of neurosis but also nearly all aspects of the psychoanalytic field in the frequently encountered psychogenic disorders are dealt with. Practically every phase — in fact almost every statement — is bibliographically covered and referentially indexed, so that there is no doubt left for the reader concerning where the weight of the opinion and experience of other workers and the author is directed.

A detailed description of the book would necessitate a repetition of the chapter headings. The development, description and therapeutic consideration of so-called "functional" emotional illnesses, however, are delivered so painstakingly and concisely that at times the reader may believe that Dr. Fenichel is giving him a personal series of lectures in these subjects. The abundantly illustrative case material does not tax the reader to find the desired examples.

Depending on the background of the reader, a certain amount of dissension may arise with the inclusion of manic depressive and schizophrenic syndromes and standard psychopathic personality pictures (character disorders) in a psychoanalytic text. The descriptions of these conditions are not presented, but the pathogenesis of each major symptom is discussed according to psychoanalytic principles. The terms used in the following typical description may be somewhat distorted so as to reflect chiefly analytic principles: "The hypertrophy of the reassuring infantile partial instinct simultaneously serves as a safeguard to maintain the repression of the Oedipus complex and of other warded off remainders of infantile sexuality." A tilt with a wooden spear is made against "constitutional determinists . . . who employ Latin neologisms" in the discussion of fixation.

Schizophrenia, as is frequently done, is dealt with as a repression, extending back, at least in part, to the narcissistic level. The important symptoms of schizophrenic psychoses are analyzed and, in a sense, genitalized. Hallucinations are considered capable of interpretation in the same way as dreams. Delusions are regarded as misjudgments of reality based on projection: " . . . representing an attempt to supplant the last parts of reality, they often contain elements of the repudiated reality . . . and portions of warded off drives as well as projected demands of the superego." Paranoia and paranoid schizophrenia are believed to differ in that in the former "a more fortunate constellation of psychological forces permits a definite encapsulation of the pathological process."

Echolalia, echopraxia and automatic obedience are also attributed to primitive attempts at regaining contact. The infantile "mimetic expressions" are considered in apposition to simultaneous "warded-off hostile impulses" and "magic gestures" indicating "desired behavior of other persons in the future." Catatonic rigidity is held to reflect a conflict between the impulse to act and the defense against it. Borderline cases are discussed without — in the reviewer's opinion — the careful directiveness that characterizes the bulk of the text; issue may be taken with the following quotation:

> . . . potential schizophrenics . . . have not broken with reality yet, though they show certain signs of beginning such a break and, under unfavorable circumstances of life, may develop into psychotics; or they are persons who have "channelized" their schizophrenic disposition, . . . eccentrics who are crazy in one more or less circumscribed area and otherwise retain normal contact with reality.

One might also question the terms "partial delusions," "partial hallucinations" and "partial stereotypies."

Aside from the perilous trip through the schizophrenic channel in which many workers have floundered, Dr. Fenichel's book is praiseworthy in all respects. The avoidance of numerous references to classic and popular dramatic literature is as refreshing as the use of well known English expressions and idioms. This is not an elementary text for popular reading but a real psychoanalytic reference book for the psychiatrist.

Men Without Guns. Text by DeWitt MacKenzie and descriptive captions by Major Clarence Worden, Medical Department, United States Army. With a foreword by Major General Norman T. Kirk, surgeon general of the United States Army. F°, cloth, 152 pp., with 137 plates. Philadelphia: Blakiston Company, 1945. $5.00.

This book is based on the work of twelve distinguished artists who were assigned to theaters of action in Europe, the Pacific, the India, Burma and China front and hospitals at home and abroad, training centers and industrial plants in the United States. The artists did their sketches and paintings on the spot. Among the subjects dealt with are the training of physicians and enlisted corpsmen, the production of medical and surgical supplies, the movement of men and supplies in combat areas, the general hospitals, including surgery, convalescence, rehabilitation and occupational therapy, the Army Nurse, the hospital ship, aviation medicine and the performance of the Medical Corps in actual combat zones. Although the artists who went to the front were in actual combat zones and were exposed to diseases of all kinds, none were injured or became ill. The humorous side is not neglected, serving as a bold relief to the serious care of the wounded and ill.

Most of the reproductions are in color and are excellent. The descriptive text is well written in an easy, narrative style and covers the Southwest Pacific, Saipan, Italy, D-Day in Normandy and the Burma Road. This work is an out-

standing graphic contribution to the medical history of World War II and should be in all libraries, public and medical.

Science and Scientists in the Netherlands Indies. Edited by Pieter Honig, Ph.D., and Frans Verdoorn, Ph.D. 4°, cloth, 491 pp., with 134 illustrations. New York: Board for the Netherlands Indies, Surinam and Curaçao, 1945. $4.00.

This collective work, in which the science of the Netherlands Indies is discussed by a number of authorities in special fields, contains some material of medical interest. Five chapters are devoted to the history of the cultivation of cinchona. There are short chapters on veterinary service, beriberi, rabies, medical research, medical education and missionary physicians and hospitals. The larger part of the text is devoted to the natural sciences and chemistry. A valuable compilation of scientific institutions, societies and research workers in the Netherlands Indies will be found in a supplement. A few contributions are written in French and German.

The work is not well arranged from the point of view of subject relation. The text is printed in two columns, and the book is too heavy for its size owing to the weight of the coated paper not required for the kind of illustrations used in the text. The type is much too small for comfortable reading. A lighter paper and larger type, although increasing the number of pages, would have produced a lighter and much more satisfactory volume. The work is valuable, however, in providing a story of science in the Netherlands Indies.

Pathology in Surgery. By N. Chandler Foot, M.D. 4°, cloth, 511 pp., with 368 illustrations and 10 plates. Philadelphia: J. B. Lippincott Company, 1945. $10.00.

Dr. Foot has written a short book on his personal experiences as a surgical pathologist. Informality in a scientific text is unusual, but it makes the book more readable. It would be almost impossible to cover the entire field of surgical pathology in less than five hundred pages that include almost four hundred illustrations, but the author has tried to do this and in addition has considered many medical conditions in which biopsies are occasionally performed, with the result that he does not do justice to some of the more important surgical lesions. For example, there is no need to spend an entire page on chronic glomerulonephritis and nephrosclerosis. Anyone interested in this subject would naturally consult a textbook on general pathology.

The title implies an exposition on the pathology seen at the operating table. In fact, the fly leaf of the book states, "It is a thorough coverage of the close relationship between the pathologist and the surgeon in the operating room. . . ." Unfortunately, the book does not emphasize this aspect because it seriously neglects gross pathology, gross descriptions of pathologic lesions, by and large, being skipped over hurriedly. This might be excused if sufficient gross illustrations were used; but of the three hundred and sixty-eight illustrations, there are only four black-and-white photographs of gross specimens and six color plates, each containing only a few colored drawings of some of the most frequent pathologic lesions, such as appendicitis, cholecystitis and cancer and cysts of the breast.

The competent surgical pathologist is the one who is able to make a diagnosis grossly in the operating room. For example, the most frequent lesion for which the pathologist is called to the operating room is a lump in the breast. The author states, in relation to tumors of the breast, that the surgeon should "cut down upon the tumor and remove a generous biopsy (if not the entire growth)" rather "than to putter with aspiration biopsies." He continues: "Should the freezing microtome produce sections that reveal cancer, the operation for radical mastectomy should then be undertaken without further delay; should a nonmalignant growth be diagnosed the wound is then closed up forthwith and the patient returned to her bed. Seldom if ever is it necessary to await the examination of permanent sections from paraffin blocks, although once in a great while a frozen section may give clinical evidence that requires further investigation." From this statement it appears that the pathologist should make frozen sections of all tumors of the breast. In the reviewer's experience most pathologists are able to make a gross diagnosis of lesions of the breast in about 90 per cent of cases, and often when the gross diagnosis is in doubt the frozen section does not help.

The emphasis throughout this book is placed on the microscopic appearance of pathologic lesions, and many of the photomicrographs are excellent. Some are poor, however, and occasionally, as in the chapter on bone marrow, the text describes many cellular details without accompanying photomicrographs.

The chapters on lymph nodes, spleen and skin contain excellent photomicrographs, and the subjects are well presented. With the increase in chest surgery one would have liked to see a fuller presentation of bronchiectasis and the mediastinal tumors. The handling of the pathology of the adrenal tumors is superficial, in contrast to the fuller discussion of their endocrine aspects. The pathology of the uterus and cervix are considered together, and the fact that their clinical, surgical and pathological features are different is not brought out.

The text is well indexed, and a good list of recent references is given at the end of each chapter.

Personality Factors in Counseling. By Charles A. Curran, Ph.D. With a preface by Michael J. Ready and an introduction by Carl R. Rogers. 8°, cloth, 310 pp., with 71 illustrations. New York: Grune and Stratton, 1945. $4.00.

The introduction and the preface of this book call to the attention of the reader the need for better interpersonal relations and the dangers implicit in the limitations of individual freedom by various autocratic social systems. A tentative promise of changing emotional disturbance into an understanding, contented, maturely deliberative status is given in twenty counseling interviews.

The text, however, without any statement of principles, methods or technics launches into what is termed a typical, nondirective counseling procedure, the author taking it for granted that the reader is aware of the fundamentals. Automatically recorded interviews are then shown to be better than written or memorized interviews. Actually, several other texts on nondirective counseling are required as a preamble to an understanding of this one. About a hundred pages of the text are devoted to a statistical consideration of the responses or statements of one case. Positive statements, indicating improvement, and negative statements, indicating no progress or regression, have been counted by "judges" and arithmetically projected on increasingly complex charts, finally to be treated by chi-square formulations, which are intended to demonstrate that nondirective counseling brought about improvement in an emotional or anxiety-laden condition. The reviewer would like to believe that personality factors, insight into conflicts and certainly expressions of behavioral adjustments could be statistically evaluated. This wish is still unfulfilled after reading this text. One might similarly count the number of times a patient refers to himself in a number of interviews and mathematically derive an "egocentric ratio," which might then be employed in comparative personality studies. The statistical features in this book seemed to be similarly syllogistic.

In studying the content of the illustrative interviews one is impressed by the fact that "the therapist" (the author) merely echoes or paraphrases what "the client" has previously said—returning the expressions in words more meaningful to "the client" and understanding (by inference) the important affective alterations in the course of the therapy. If this is nondirective counseling, it should be as clearly stated as the suggestions or implicit assurances that improvement is noticeable. It is indeed distracting to note the avoidance of the terms "patient" and "illness" in the consideration of what, on the evidence presented, could very well have been neurotic anxiety and other emotional disorders. The lack of mention of any presenting psychosexual conflict would be amazing if the counseling were not maintained on a superficial level.

In spite of the foregoing the reviewer is cognizant of the author's unlimited patience and considerable knowledge of and rapport with the more important human emotional modalities. The author's counseling ability is known to be equaled by that of few people. It would have been more instructive for a man of his caliber to have written a book that abounded with much case material and a description of how nondirective counseling brought about a solution to presenting symptoms. Instead, this is a conglomeration of severely involved statistical formulations with their implications for future personality studies.

The reviewer believes that it is essential to delineate sharply the respective spheres of medical and nonmedical psychotherapeutic efforts. When can "a client" be classified as "a patient"? When does "a counselor" practice psychiatry without a license? Admittedly, even tritely, there is a lack of trained psychiatric personnel. This may not be the reason for the independent undertaking of rather extensive psychotherapy by nonmedical workers. That people take their troubles to anyone with a sympathetic ear has led to popularized concepts of counseling by such personages as Mr. Anthony and his imitators, the listening to troubles being thus made a financial enterprise. The dangers of such popular inclinations should be pointed out, standards planned and licenses issued accordingly.

With all the above in mind, this book can be of interest to statistically minded students of human emotions and behavior. To the average psychiatrist or to allied professional personnel, probably too much effort will be required in reading to make it useful.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Suggested School Health Policies: A charter for school health. Second edition. Revised by the National Committee on School Health Policies of the National Conference for Cooperation in Health Education. 8°, paper, 46 pp. New York and Minneapolis: Health Education Council, 1946. 25 cents.

This pamphlet, which is written as a guide for all concerned in school health, integrates the viewpoints of many professional groups on the contributions that school programs can make for the health of children and communities. The National Committee on School Health Policies consists of fifteen representatives of fifteen different educational, medical, social and public-health organizations. Eight of these organizations are medical in character, and the chairman of the committee is Dr. Charles C. Wilson. The program is an outline of six main divisions, as follows: provisions for healthful school living; health and safety instruction; services for health protection and improvement; health aspects of physical education; education and care of the handicapped; and qualifications of school-health personnel. There is a preliminary chapter on general health policies. The pamphlet includes suggestions for a school program. Appended to the text is a selective source bibliography on the various aspects of the subject. This pamphlet is recommended to all persons concerned with public health in the schools. It should also be in all public-health libraries.

A Malariologist in Many Lands. By Marshall A. Barber, A.M., Ph.D. With a foreword by Paul F. Russell. 8°, cloth, 158 pp. Lawrence, Kansas: University of Kansas Press, 1946. $2.50.

In this popular book Dr. Barber informally tells the story of his travels and experiences in the war against malaria. He has been chasing malaria plasmodia and their anopheline vectors for half a century in the United States, Central and South America, Europe and Asia. To Dr. Barber belongs the credit for discovering the effectiveness of Paris green as a larvicide. In conjunction with Justice B. Rice, he improved a cumbersome and laborious precipitin test so that it could be used rapidly and cheaply to determine the source of blood meals of thousands of mosquitoes. This basic work made it feasible to measure on a large scale the amount of contact between Anopheles and man, and thus to focus attention on the one or two species chiefly responsible for spreading malaria in any given region. In conclusion, Dr. Barber states that the amount of malarial illness rivals that of any other disease, except perhaps the common cold. He believes that all dwellings should be screened at night as a protection against the entrance of mosquitoes. A significant aspect of the book is the way in which it shows how the prevalence of malaria is related to environmental factors, such as flood, famine, irrigation and the presence of wild animals. The book is written in an informal, easy style and should find a place in all public and medical libraries.

NOTICES

ANNOUNCEMENTS

Dr. Archie A. Abrams calls attention to the omission of his office address and telephone number from the current telephone directory. His office is at 1093 Beacon Street, Brookline, and the telephone number is ASPinwall 8951.

Dr. Albert H. Covner announces the opening of his office, with practice limited to diseases of the heart, at the Hotel Breakers, 285 Lynn Shore Drive, Lynn.

Dr. W. Philip Giddings announces the opening of an office for the practice of general surgery at 266 Beacon Street, Boston.

Dr. Harry Portman announces his return from military service and the opening of his office for the practice of medicine at 769 Salem Street, Malden.

HOSPITAL RESEARCH COUNCIL

A meeting of the Hospital Research Council will be held in the Bigelow Amphitheater of the White Building, Massachusetts General Hospital, on Tuesday, February 25, at 4:30 p.m.

PROGRAM

Competition of Antitoxin and Lecithin for *Clostridium welchii lecithinas*. Drs. P. Zamecnik and F. Lipmann.

The Effect of Oral Streptomycin on the Intestinal Flora. Dr. L. W. Kane.

Disseminated Encephalomyelitis Experimentally Produced by the Use of Homologous Antigen. Dr. L. Raymond Morrison.

The Excretion of 11-oxycorticosteroid-like Substances by Normal and Abnormal Subjects. Drs. N. B. Talbot and F. Albright.

TUFTS MEDICAL ALUMNI ASSOCIATION

The annual medical alumni lecture will be presented at Tufts College Medical School on Wednesday, March 5, at 4:00 p.m. Dr. Curtiss B. Hickcox, professor and head of the Department of Anesthesiology, Temple University School of Medicine, will speak on the subject, "Development of Anesthesiology and Its Relation to Medicine in General."

AMERICAN CHEMICAL SOCIETY

A symposium "Antibiotics," with Dr. Chester S. Keefer serving as chairman, is included in the program of the coming meeting of the Northeastern Section of the American Chemical Society. This particular exercise will be held in Room 10-250, Massachusetts Institute of Technology, at 4:05 p.m. on Thursday, March 13. The first paper, "The Role of Antibiotics in Medicine," will be given by Dr. Keefer; the second, "Penicillin: Chemistry and synthetic approaches," by John T. Sheehan of the Massachusetts Institute of Technology; and the third, "The Discovery and Development of Streptomycin," by Selman A. Waksman, of Rutgers University. A general discussion and questions will follow.

AMERICAN SOCIETY FOR THE STUDY OF STERILITY

The third annual convention of the American Society for the Study of Sterility will be held at the Hotel Strand, Atlantic City, New Jersey, on June 7 and 8, 1947. The general theme of the meetings will be that of attempting to disseminate to the physician treating marital infertility an overall picture of the latest advances in reproduction. The convention will include original papers, round-table discussions, scientific exhibits and demonstrations. Registration for the sessions is open to members of the medical and allied professions. Additional information may be obtained from the secretary, Dr. John O. Haman, 490 Post Street, San Francisco 2.

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